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TERATOID CYST OF THE HYPOPHYSIS*

J. H. GLOBUS, M.D.

NEW YORK

Among the cystic tumors of the brain is a small group of neoplasms which, through their relation to the pituitary body or through pressure on it and adjacent structures, give rise to signs of disturbance of pituitary function and thus acquire an especial clinical interest.

Such cysts have, in the past, been variously described as cholesteatomas, dermoids, epidermoids, and, occasionally, because of the occurrence of cartilage and bone in their walls, as teratomas.

The finding of cholesterin crystals in the interior of such cysts led Mueller[1] to name them cholesteatomas. Virchow,[2] however, later rejected this term on the ground that the cholesterin crystals are not constant, and, when present, are simply the product of a degenerative process. He advocated a return to the old term of Cruveilhier "Tumeurs Perlées" (Perlgeschwülste).

Various hypotheses concerning the origin of these tumors have been advanced. Virchow believed them to arise by methaplasia from the pial or dural connective tissue. This view was opposed by Remak (cited by Erdheim) who thought that they were a variety of dermoid. Bonorden[3] described a cyst in the vicinity of the olfactory nerve which was lined by stratified squamous epithelium in which he found many spherical, concentrically arranged collections of squamous epithelial cells, forming structures not unlike epithelial pearls. Underneath this epithelial lining were groups of sebaceous cells arranged in lobules and supported by interstitial connective tissue. The tumor in his opinion corresponded in structure to the so-called cholesteatomas and he concluded that it was ectodermal in origin because of the

* From the department of pathology and the neurologic service, Mount Sinai Hospital, New York.

* Work carried out during the tenure of the Sachs Fellowship in Neuropathology.

* Read before the New York Neurological Society, Jan. 10, 1922.

1. Mueller, Johannes: Ueber den feineren Bau and die Formen der krankhaften Geschwülste, Ed. 1, 1838, p. 50.

2. Virchow, Rudolph: Ueber Perlgeschwülste (Cholesteatoma Mueller), Virchows Arch. f. path. Anat. **8**:371, 1855.

3. Bonorden: Ueber ein meningeales Cholesteatom mit Haaren und Talgdrüsen, Beitr. z. path. Anat. u. z. allg. Path. **11**:593, 1892.

presence of epidermal derivatives, such as sebaceous glands and squamous epithelium. He suggested as possible sites of origin of those tumors the point of closure of the primitive medullary tube, Rathke's pouch and then hypophyseal duct.

Beneke [4] maintained that the so-called meningeal cholesteatomas arise from the endothelial lining of the meninges. He based his opinion on the fact that by the employment of a silver stain he was able to demonstrate a strong similarity in the outline of the cells lining the cyst cavity and that of endothelial cells.

Later, however, he [5] revised this opinion, accepting the view that some of these tumors, particularly those which contain hair and sebaceous glands, have an epidermal derivation, whereas a smaller group are of endothelial origin. He then suggested the division of such cholesteatomatous cysts into three groups: (1) meningeal dermoids containing hair and sebaceous glands, resulting from embryonal displacement of the skin; (2) meningeal endothelial-pearl tumors, free from hair and sebaceous glands, derived from the endothelial lining of the meningeal trabeculae, and (3) meningeal epidermoids free from hair and sebaceous glands, derived from misplaced epidermoid epithelial cells.

Bostroem [6] in 1897 undertook the study of the histologic character of cholesteatomas with a view to determining their nature and origin. He decided in favor of the epidermoid character of such neoplasms. He laid particular emphasis on the work of Wilms,[7] who had shown that dermoid cysts of the testes and ovaries almost always contain derivatives of all three germinal layers, and can be considered as true embryomas, differing from dermoid cysts elsewhere. The latter are bigerminal in origin and contain only ectodermal and mesodermal components.

He found further support for this conception in the fact that, coincident with the formation of the primary and secondary brain vesicles, there is a histogenetic change taking place in the adjacent enveloping ectoderm and mesoderm and that these zones of constriction of the medullary tube are the most constant sites of such tumors. These locations, in his opinion, are most favorable for embryonal misplacement of epidermis which may later develop into cholesteatomas. When, however, such epidermal nests give rise to new growths, the

4. Beneke: Zur Frage der meningealen Cholesteatome, Virchows Arch. f. path. Anat. **142**: 1895.

5. Beneke: Zur Frage der meningealen Cholesteatomen und Berichtigung, Virchows Arch. f. path. Anat. **149**:95, 1897.

6. Bostroem: Ueber piale Epidermoide, Dermoide und Lipome und durale Dermoide, Zentralbl. f. allg. Path. u. path. Anat. **8**:1, 1897.

7. Wilms: Die teratoiden Geschwülste des Hoden mit Einschluss der sogenannten Cystoide und Enchondrome, Beitr. z. path. Anat. u. z. allg. Path. **19**:233, 1896.

resultant cysts should be grouped with the epidermoids; but when they contain connective tissue elements of the skin as well, they should be considered as dermoids.

Further light was thrown on the character and origin of cholesteatomas by the exhaustive work of Erdheim.[8] His attention was directed mainly to the cysts which are found at the base of the brain, in the vicinity of the hypophysis, and which present, most commonly, a direct connection with some portion of the pituitary body. Such tumors have been frequently described as infundibular cysts, cystosarcomas, carcinomas, and, occasionally, as papillomas. These cystic tumors bear a strong resemblance to the so-called cholesteatomas because of their squamous epithelial lining, the presence of cholesterin crystals and the appearance in the lining membrane of pearlike structures. Occasionally, bone and foreign body giant cells are found in their walls. These tumors are usually well circumscribed and rarely invade the adjacent brain tissue. It is always possible to demonstrate in such tumors some connection with the pituitary, most often with the infundibular process. Erdheim's previous discovery of epithelial cell remnants in the thyroid region, in connection with the subinvoluted thyroglossal ducts, led him to suspect a parallel condition in the hypophysis. He first studied normal hypophyses and showed that in about 80 per cent. of normal glands, small numbers of squamous epithelial cells were to be found on the anterior surface of the anterior lobe. He traced these epithelial rests to the subinvoluted craniopharyngeal duct of the hypophysis. He then concluded that all so-called cystic cholesteatomas occurring in connection with the pituitary are derived from the subinvoluted remnants of the hypophyseal duct, and designated them as hypophyseal duct neoplasms. He separated these tumors from the epidermoids of Bostrom by pointing out some differences in the gross anatomic relationship and variations in the histologic structure. The epidermoids, being true derivatives of the skin, he believed to give constantly the keratohyalin reaction in their epithelial cells, as well as other evidence of cornification. Hair and sebaceous glands and intercellular bridges between the squamous epithelial cells are also found. In the hypophyseal duct tumors he failed to get the keratohyalin reaction, and did not find hair follicles or subaceous glands.

Erdheim, while crediting Bonorden with the early suggestion that there existed a definite relationship between cholesteatomas and the primitive buccal ectoderm, noted Bonorden's failure to substantiate this idea by actual histologic observations. He also disagrees with Bonorden's interpretation of the buccal ectodermal origin of all meningeal cholesteatomas, since misplaced epidermis associated with

8. Erdheim, J.: Ueber Hypophysenganggeschwülste und Hirncholesteatome, Sitzungsb. d. k. Akad. d. Wissensch. **113**: 1904.

embryonic development of the hypophysis will only explain the origin of such cysts as are found in the vicinity of the hypophysis and will not explain the origin of cysts found elsewhere. He also asserted that up to that time no epidermoid cyst of the hypophysis had been described, and that this serves as further proof of a distinct origin of the cysts occurring in connection with the hypophysis. He admits that, though the latter are also derived from ectoderm, they are not epidermal in origin, and, for that reason, they are not to be regarded as cholesteatomas, which must show their epidermoid character by the presence of keratohyalin and by evidence of cornification.

D'Orsay Hecht [9] reported a case which showed striking similarity in its histologic character, anatomic relationships, and in the resulting clinical manifestations, to the case here reported. The microscopic study by Herzog of the tumor of this case demonstrated it to be composed of a variety of tissues. The parenchyma was mainly made up of what was thought to be derivatives of the anterior lobe of the hypophysis. There were numerous cells, apparently similar in structure to the cells of the anterior lobe, and there were groups of cells which by their outline and their lamellated concentric arrangement simulated epithelial pearls. There were also small ducts lined by cuboidal epithelium, and filled with a colloidal substance. In addition, there was found osteoid tissue with typical bone corpuscles and haversian canals. These findings indicate, however, that only two primitive germinal layers have contributed to its formation. Thus the tumor cannot be grouped with the true teratomas.

Ehlers [10] reported a case which he considered to be an epidermoid cyst of the hypophysis because of the presence of keratohyalin granules.

Lewis [11] recorded a tumor of the hypophysis, which he considered to have originated from the intermediate lobe of the hypophysis because, in addition to the squamous epithelial pearls, he found numerous cells characterized by clear refractile cytoplasm, similar to the cells found in the intermediate lobe of the normal hypophysis.

Jackson [12] described a cyst of the hypophysis and concluded that tumors derived from the embryonal tissue along the course of the craniopharyngeal duct have not received proper recognition. He emphasized that tumors belonging to the hypophyseal duct group are always found in the median line at the base of the brain, bounded in

9. Hecht, D'Orsay: A Teratoma of the Hypophysis, J. A. M. A. **52**:1001 (April 8) 1909.

10. Ehlers, H. W. E.: Ein Beitrag zur Kenntniss der Infundibularzysten des menschlichen Gehirns, Virchows Arch. f. path. Anat. **199**:542, 1910.

11. Lewis, D. D.: A Contribution to the Subject of Tumors of the Hypophysis, J. A. M. A. **55**:1007 (Sept. 17) 1910.

12. Jackson, Harry: Craniopharyngeal Duct Tumors, J. A. M. A. **66**:1082 (April 8) 1916.

front by the optic chiasm and posteriorly by the pons. The hypophysis is usually intact, though it may be pressed against the floor of the sella. There is always an intimate connection between the tumor and the infundibulum. The first five cranial nerves are frequently involved. The cysts usually contain serous, mucous or hemorrhagic fluid, in which cholesterin crystals are often found. The inner wall of the cyst often shows papillary excrescences. Embryonal connective tissue and cells with intercellular bridging are also found.

Kanavel and Jackson [13] reported three cases of cysts of the hypophysis, and believe that such cysts are legitimate operative risks.

The contribution of Duffy [14] is of particular interest. In one of the several cases studied, he found structures believed to be derived from the pars intermedia in the wall of the cyst. These were gland-like structures lined by cuboidal or columnar epithelium and filled with a colloid substance. In addition, he found, in the substance of the growth, foreign body giant cells, cholesterin crystals, epithelial pearls, mucous connective tissue, calcified vessels and giant cells enveloping dying epithelial pearls.

In another tumor, in addition to the squamous epithelium and pearls, Duffy reports the presence of cells, sebaceous in character, and intercellular bridging of the epithelium. He believes that lipoid materials from the cells are the source of the cholesterin crystals and that the latter stimulate the formation of foreign body giant cells. True bone with haversian canals was also present. The lack of actual typical skeletal bone formation he believes militates against the origin of such bone from true bone anlage.

This survey indicates the tendency of the more recent investigators, beginning with Erdheim, to single out one type of cholesteatoid cyst at the base of the brain, which because of its anatomic relationship to the hypothalamic region and because of its histologic features is thought to be derived from the remnants of the hypophyseal duct, and for this reason is designated as a hypophyseal duct tumor. There is also a tendency to distinguish this type of neoplasm from the dermoids and epidermoids of Bostroem, since they often fail to show keratohyalin granules in the lining epithelium. The absence of hair follicles in such neoplasms serves as another point of differentiation from dermoids elsewhere in meninges of the brain.

The tumor herewith reported presents many of the features common to the cystic hypophyseal duct tumor, but it is also related to the meningeal dermoids of Bostroem, as it contains keratohyalin granules and hair germs.

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13. Kanavel and Jackson: Cysts of the Hypophysis, Surg., Gynec. & Obst. **26**:61-70 (Jan.) 1918.

14. Duffy, W. C.: Hypophyseal Duct Tumors, Ann. Surg. **72**:537 (Nov.), 725 (Dec.) 1920.

The case is also believed to be of importance from a physiologic point of view, for it bears out some of the conclusions reached by Bailey and Bremer [15] in their experimental work on the pathogenesis of diabetes insipidus. They were able to show that lesions in the postinfundibular portion of the hypothalamus, and not modification of the posterior lobe of the pituitary, are responsible for the more manifest symptoms of the disease, such as polydipsia, polyuria and cachexia. It will be seen that in the case here recorded the pituitary gland showed no changes of pathologic significance, while the floor of the third ventricle and with it the postinfundibular region of the hypothalamus were markedly distorted, if not completely destroyed.

REPORT OF CASE

History.—A girl, aged 6 years, who had had no previous illness and had been quite normal up to the time of the onset of symptoms, six months before admission to the hospital, became markedly constipated. Sleep became disturbed, she became restless, lost her appetite and experienced constant thirst, demanding water frequently. Several weeks later, on consulting a physician, the diagnosis of diabetes was made, and the child was treated accordingly. With the increase of thirst and increase of water intake, there was an increase in volume and frequency of urination. The child was losing strength, and would frequently complain of fatigue; she gave up playing, became irritable, and finally became confined to bed because of constant headaches and general weakness. A week before admission, it was noted that the child's mouth was drawn to one side, and her left shoulder drooped and twitched frequently. She was admitted to the hospital with the complaint of headache, fatigue, excessive thirst, enuresis, loss of appetite and weakness of the left shoulder.

Physical Examination.—The patient was fairly well nourished and somewhat undersized, with a profuse growth of lanugo hairs all over the body. There was ptosis of the right eyelid and external strabismus of the right eye. The left pupil was larger than the right. Both pupils reacted to light and during accommodation. There was left facial weakness and slight weakness of the left arm and hand. The latter was held in the hemiplegic position. There was slight weakness of the left leg. The deep reflexes were more active on the left side than on the right, though generally reduced. The Babinski reflex was doubtful, but gait and station were normal. The abdominal reflexes could not be elicited. The spinal fluid was negative. The diagnosis of neoplasm involving the posterior lobe of the pituitary and the right crus cerebri was made.

Necropsy Findings (Examination of the brain only was permitted).—The exposed dura was normal in thickness and without demonstrable epidural or subdural hemorrhages. The underlying pia-arachnoid was markedly edematous and of a purple hue. The convolutions of the brain were definitely flattened and compressed. On raising the frontal lobes a large purple, fluctuating mass presented itself at the base of the brain. It covered the optic chiasm, to which it was adherent (Fig. 1). Posteriorly, it filled up the entire interpeduncular space. Its bulging inferior and partially free surface was prolonged into a

15. Bailey, Percival, and Bremer, Frederic: Experimental Diabetes Insipidus, Arch. Int. Med. **28**:773 (Dec. 15) 1921.

funnel-shaped process, which seemed to be continuous with the pituitary body. The latter was extremely small in size, compressed, and was lodged in a shallow and eroded sella turcica. The base of the superior surface of this mass was firmly implanted in the substance of the brain. The optic chiasm and tracts were flattened.

Fig. 1.—Ventral surface of the brain, with a cyst occupying the entire interpeduncular space.

The tuber cinereum and the mammillary bodies could not be identified since the floor of the third ventricle was stretched and flattened by the tumor mass, which almost obliterated the cavity of the third ventricle. The cerebral peduncles were displaced laterally and were reduced in size. This was particularly pronounced on the right side. During the process of detachment of the brain from the base of the skull, the neoplasm was punctured and a dark-brown, granular, semifluid mass escaped from the cavity. On opening the

latter more fully, it collapsed, and it was then noted that it was a rather thin walled cyst, lined by a corrugated membrane which was studded with numerous small, glistening elevations. Cholesterin crystals were demonstrated in the contents of the cyst. The cyst was 4 cm. in length and about 3.5 cm. in width. It had stretched markedly the vessels constituting the circle of Willis, particularly the posterior communicating and anterior cerebral vessels (Fig. 1).

The third nerve on the right side was compressed and flattened by the neoplasm. A horizontal, longitudinal section of the brain gave a still better

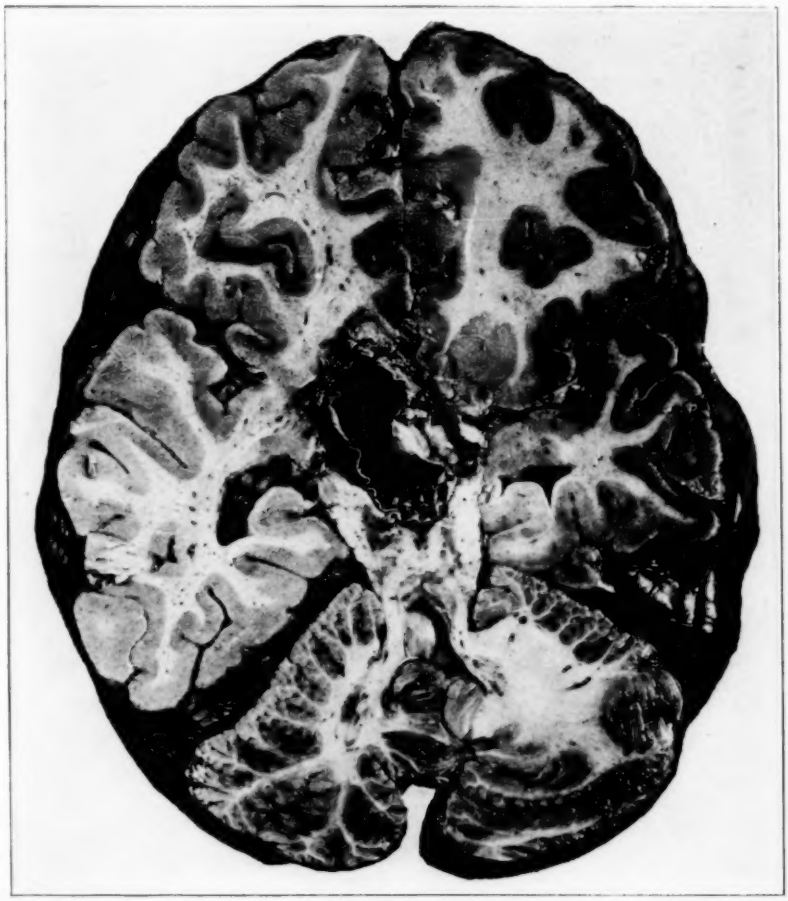

Fig. 2.—Section of the brain, showing the cavity of the cyst, the small cartilaginous mass projecting into the cavity, and the lateral displacement of the cerebral peduncles.

view of the gross structural changes that were brought about by the neoplasm (Fig 2). The cavity of the cyst was fully exposed and its inner wall was disclosed. The lining of the cyst gave the appearance of a mucous coat. At the left anterior portion of the cyst, the wall was thickened, giving rise to a tuberous elevation, cartilaginous in consistency, and somewhat translucent in appearance.

Microscopic Anatomy.—From the gross appearance of the neoplasm it was evident that little variation would be found in its makeup, except for the small cartilaginous nodule described above.[16]

The wall of the cyst was fairly uniform in thickness and showed also a more or less uniform histologic structure. It was composed of three layers. The innermost coat, a layer of stratified squamous epithelium, showed, at a few points, slight variation in the character and stage of development of its epithelium (Fig. 3). The middle layer consisted of loose connective tissue in which were embedded numerous glandular acini and many small ducts. The

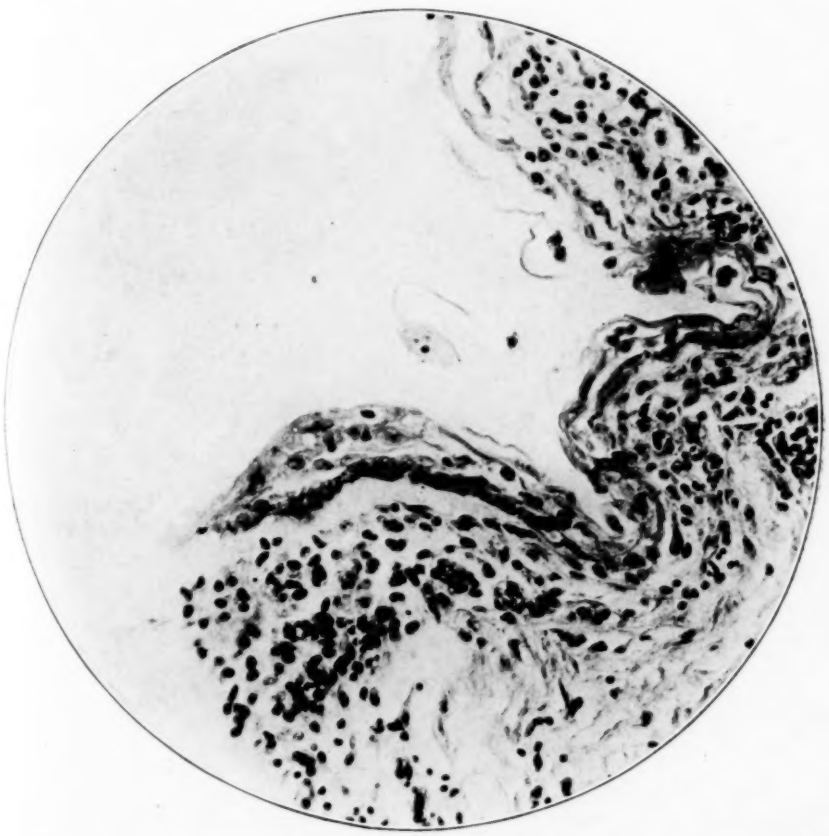

Fig. 3.—Photomicrograph of the inner lining of the cyst, showing the embryonal character of the stratified squamous epithelium; × 240.

16. In order to make sure of this relative uniformity of the tumor structure, about twenty blocks were taken from various parts of the cyst, including several blocks of tissue from the cartilaginous mass. These were embedded in paraffin, cut in sections of various thickness and stained by such methods as hematoxylin-eosin, Heidenhain's iron-hematoxylin, van Gieson's, and Weigert's keratin stain. Sudan III and scharlach R were employed in staining frozen sections.

glands strongly resembled salivary glands and the ducts were lined by tall cuboidal epithelium. The lumen of these ducts was filled with a pink staining colloidal substance. The third and outermost layer was composed of a fairly thin stratum of dense fibrous connective tissues.

The squamous epithelium was of particular interest. This lining showed a strong resemblance to the dermis of an embryo (Fig. 3). It consists of three layers: the outer, corresponding to the epitrichium, the middle or intermediate layer and the lowermost or the stratum germinativum. Here and there

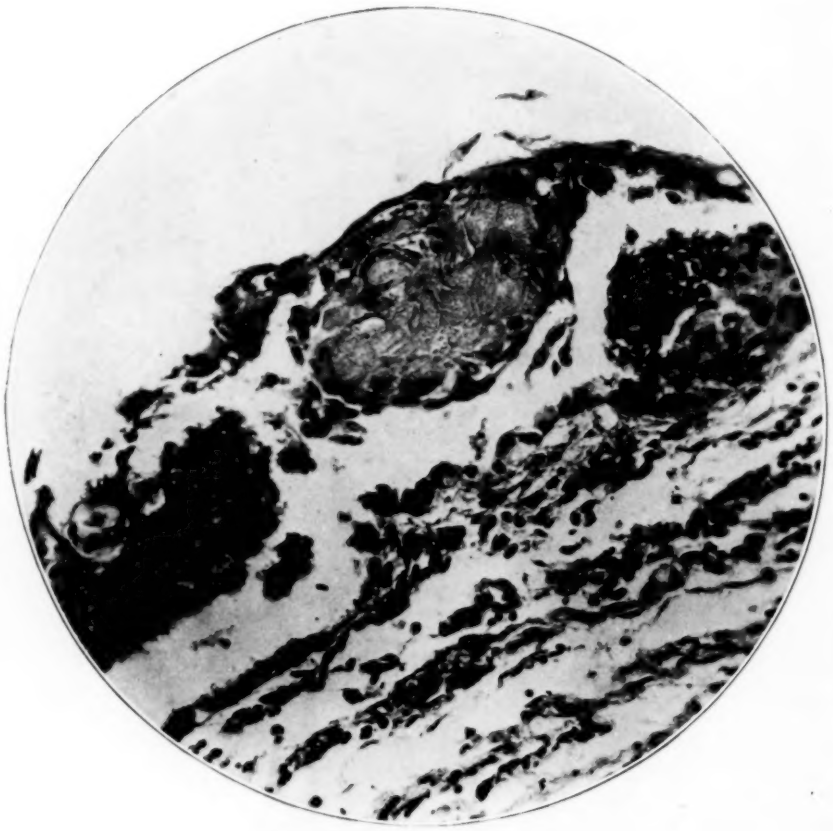

Fig. 4.—Photomicrograph showing well defined hair germs on either side of a group of degenerating squamous epithelial cells.

larger collections of cells composed mainly of the germinal layer gave the appearance of hair anlages (Fig. 4). Another feature of interest was the accumulation of deeply staining epithelial cells arranged in concentric layers, giving rise to structures not unlike epithelial pearls (Fig. 5). The cells in the center of these pearls appeared to have undergone degeneration, while the peripheral cells have retained the structure of basal cell epithelium and show, when stained with iron-hematoxylin, the characteristic intercellular bridges;

when stained with Weigert's keratin method, a blue color was imparted to these cells, giving evidence of the presence of kerato-hyalin. These collections of epithelial cells were on the free surface of the cyst.

On studying the small cartilaginous mass in the wall of the cyst, there were found several types of embryonic tissues of mesodermal origin, such as embryonal cartilage, mucous connective tissue, young fibrous tissue, newly formed bone, with typical bone corpuscles, calcified trabeculae, endosteum and periosteum crowded with numerous osteoclasts, osteoblasts and osteophytes. Mar-

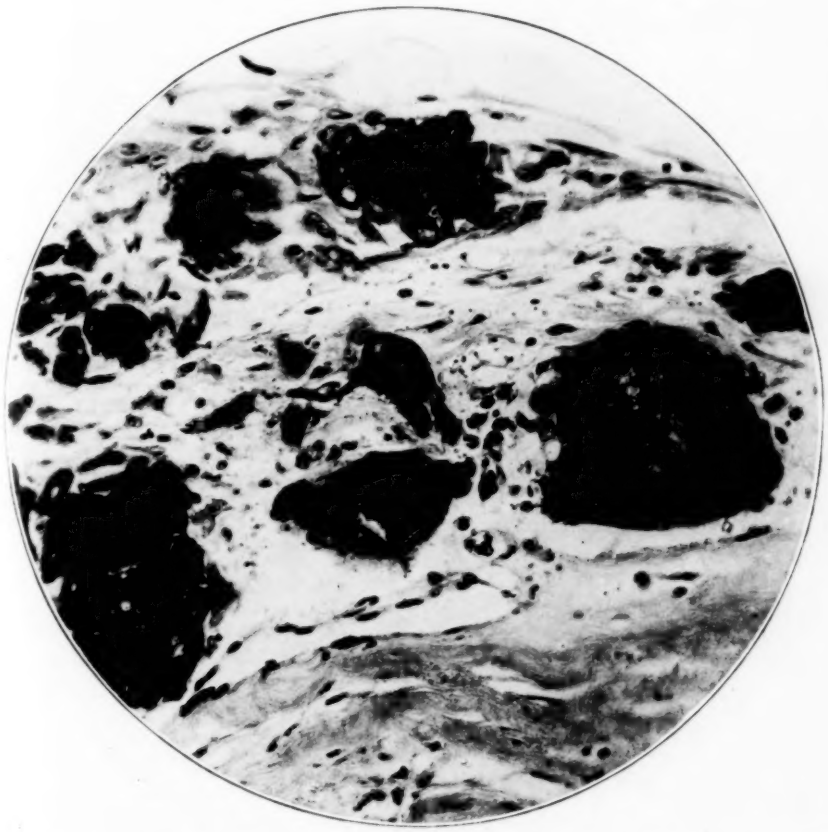

Fig. 5.—Photomicrograph showing the epithelial pearl-like structures in the innermost coat of the wall of the cyst; × 300.

row cells filled with yellow granules, which gave a typical iron reaction, were also found. In addition to the structures noted, there was a collection of cells arranged in long cords and supported by a fine reticulum of connective tissue which, when stained by specific fat stains, were seen to be filled with large fat globules. These cells were first considered to be young embryonic fat cells, but because of the pyknotic character of the nuclei and the irregularity in the fat globules, they were finally thought to be similar to the cells found in sebaceous glands (Fig. 6).

Summary.—The tumor was a centrally situated, unilocular cyst, filled with dark brown, coarse, granular material. Its interior was lined by corrugated mucous membrane, on the surface of which were yellowish glistening papillary elevations. It bore a very intimate relationship to the hypophysis, being apparently attached to the infundibular process. Microscopically, it had a stratified squamous epithelial lining which was embryonal in character. Here and there on the surface of the epithelial lining, there was a heaping-up of cells which had a concentric lamellated arrangement, giving the appearance of epithelial

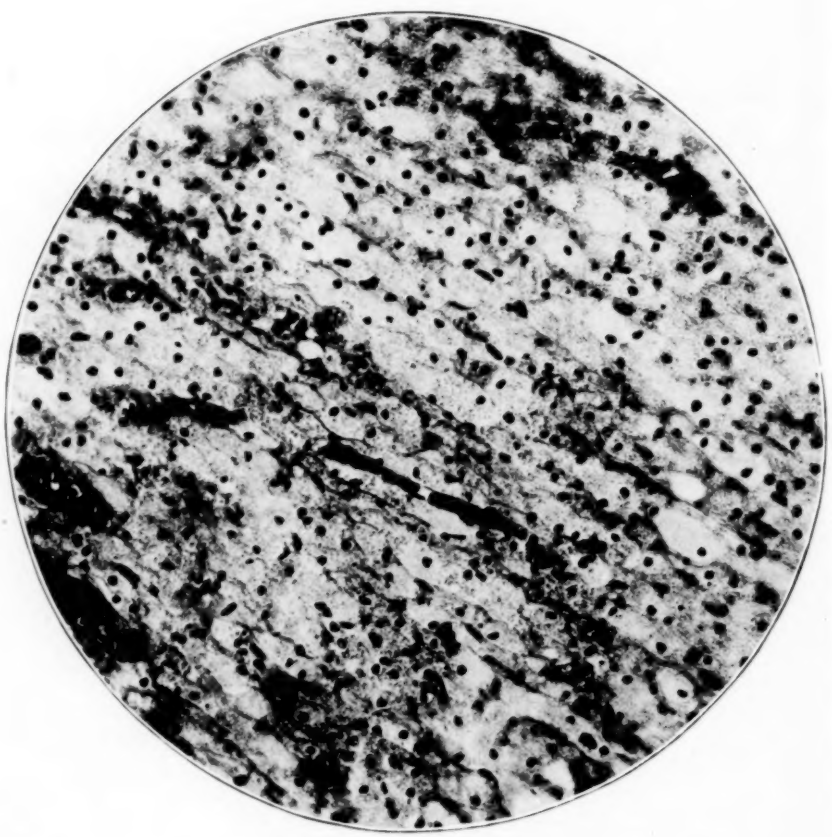

Fig. 6.—Photomicrograph of section through the small cartilaginous mass, showing cells similar to sebaceous gland cells, arranged in cords; ×240.

pearls. The latter were in various stages of degeneration, showing central areas of calcification, and were frequently surrounded by foreign body giant cells. Beneath this epithelial lining, there was a connective tissue stroma, in which glandular tissue, of both salivary and sebaceous types were found.

The tumor also contained embryonal cartilage, dense fibrous tissue, embryonic mucous tissue, and bone, representing all the osteogenetic elements. Keratohyaline granules were demonstrated in squamous epithelial lining and

developing hair follicles were present in the form of hair germs. It is evident that this tumor presents in its structure all the elements of the ectodermal and mesodermal components of the primitive skin, to which other embryonal tissues of mesodermal origin (bone, cartilage, mucous connective tissue) are added. While it is quite possible that the calcified trabeculae and the osteogenetic elements are the result of metaplasia in a degenerated area, the hair follicles and sebaceous cells could not have had this origin. We are, therefore, dealing here with a growth which is bigerminal in character and not a true teratoma.

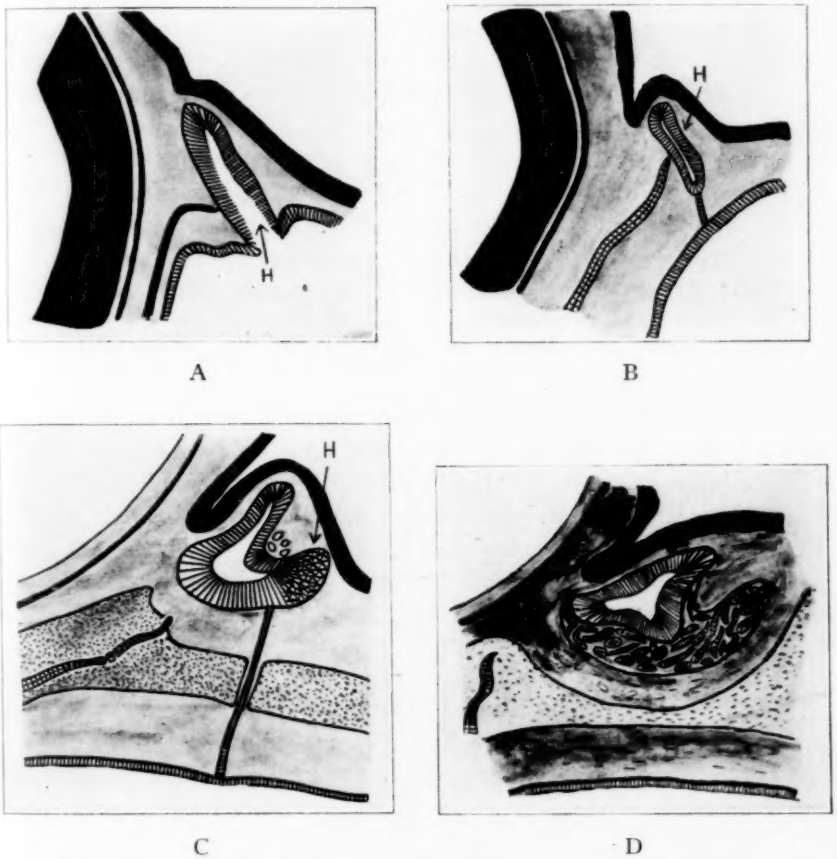

Fig. 7.—A series of diagrams illustrating the development of the hypophysis: *A*, invagination of the buccal ectoderm, giving rise to the so-called "Rathkes" pouch (*H*), communicating with the primitive oral cavity by the craniopharyngeal duct; *B*, Rathke's pouch which has assumed the form of a closed vesicle, with a solid cord of epithelium connecting the oral cavity with the hypophyseal vesicle; *C*, the anterior lobe of the hypophysis (*H*) beginning to differentiate in its anterior portion. The solid cord, representing the involuting craniopharyngeal duct, is still present, but is being surrounded by masses of cartilage and developing bone; *D*, complete involution of the craniopharyngeal duct. The anterior lobe of the hypophysis is beginning to gain its final glandular structure.

In comparing this neoplasm with those described by Erdheim, who believes the subinvoluted craniopharyngeal duct to be the origin of such tumors, we find that there is striking similarity between the teratoid cyst here reported and his cysts derived from the hypophyseal duct. The only difference is that he failed to find hair follicles or keratohyalin granules in the epithelial lining, while these structures were found in the tumor here described. Erdheim lays emphasis on the keratin reaction, suggesting that the presence of this substance will differentiate between tumors derived from the subinvoluted hypophyseal duct and the dermoids described by Bostroem. The hypophyseal duct tumors did not show hair follicles or keratohyalin granules while these were constantly present in the dermoids. This differentiation has already been disputed by Ehlers,[10] who described a tumor similar to ours in which he was able to demonstrate keratohyalin material.

Ehlers came to the conclusion that in spite of the intimate relation of the tumor to the infundibulum and the possible origin of such a tumor from the primitive oral cavity, the presence of keratohyalin places this tumor with the dermoid cysts. He also suggested that the failure of Erdheim to demonstrate keratin can be accounted for by the method of fixation, as some of them had been kept for many years as museum specimens.

Bailey and Bremer[15] have shown that the clinical symptoms of diabetes insipidus, such as polyuria and polydipsia, can be provoked with certainty by a lesion produced in the postinfundibular region of the hypothalamus and that the removal of the posterior lobe of the hypophysis does not lead to the permanent production of such symptoms. They conclude that there is no evidence supporting the older views which assert that a hypophyseal lesion is responsible for the symptoms of diabetes insipidus. The case here reported offers further support for the views expressed by the foregoing authors, for polydipsia and polyuria were striking symptoms late in the course of the disease and the anatomic findings showed that the pituitary gland was intact though somewhat compressed, but the hypothalamus was distinctly involved.

CONCLUSIONS

1. The histologic features of the tumor place it among autochthonous teratoid cysts.

2. Though the tumor probably had its origin from the lining of the primitive oral cavity, there is no histologic justification for placing it in a group distinct from other meningeal dermoids.

3. The occurrence of symptoms of diabetes insipidus in these hypophyseal duct tumors is probably referable to destruction in the hypothalamic region and not to destruction of the hypophysis itself.

CHARCOT-MARIE ATROPHY: THE REPORT OF A CASE WITH NECROPSY*

CHARLES S. POTTS, M.D., AND GEORGE WILSON, M.D.

PHILADELPHIA

Cases of Charcot-Marie atrophy with necropsy are sufficiently rare to warrant report. To date, six cases of this condition with the pathologic findings have been recorded; that reported by one of us (G. W.) is the only example from this country. The pathologic findings in the six cases have not been entirely uniform; all of them showed degeneration in the posterior columns, and in four of the six cases the peripheral nerves were diseased; in one slight degeneration was found in the peroneal nerves alone, and in one the nerve trunks were normal though the intramuscular filaments were altered. The anterior horn cells were greatly involved in one case, but the other five cases showed little alteration in the structure of these cells. Clark's columns were moderately affected in one case. The pyramidal tracts showed slight changes in two cases.

REPORT OF A CASE

Clinical History.—M. R., a single woman aged 51, was admitted to the Philadelphia General Hospital on July 9, 1914. At that time a note was made that a history could not be obtained because of the mental condition of the patient. In 1918, the history of M. R. which follows was obtained from her mother: The father died from unknown cause at the age of 38. The patient is one of five living children, aged respectively 60, 58, 57, 51 and 48 years. One child died in spasms when 18 months old and the mother had one miscarriage. No member of the family had had symptoms similar to those of the patient. She had the usual diseases of childhood, was bright, and received a common school education. As a child her legs were weak and she had to be helped up and down stairs by members of the family. She assisted with the housework but was never employed outside the home. Two years before going to the hospital she became bedridden and apparently suffered severe pain.

On July 26, 1918, one of us (C. S. P.) examined the patient and found: The woman was deficient mentally and unable to give a history of her illness. Vision appeared to be good and the cranial nerve functions were normal with the exception that a moderate degree of deafness was present. The pupils were contracted, irregular, and did not react to light, but reacted well in accommodation. The eyegrounds were normal. The patient was unable to walk or to feed herself. All movements of the arms could be made, though with diminished strength, but there was very little movement of the hands or fingers.

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* From the Neurological Service and the Laboratory of the Philadelphia General Hospital and from the School of Medicine of the University of Pennsylvania.

* Reported at a meeting of the Philadelphia Neurological Society, Dec. 19, 1919.

Hyperextension was present at the metacarpophalangeal joint of all fingers except the index fingers; the second and third joints of all the fingers were flexed. The fingers, with the exception of the little and ring fingers of the left hand, could be passively straightened. The muscles of the shoulder girdle and arms were slightly atrophied; atrophy was much more intense below than above the elbows and fibrillary twitchings were present in the muscles of the forearms. The muscles of the back were well developed. Slight

Fig. 1.—Section of the second lumbar segment of the spinal cord.

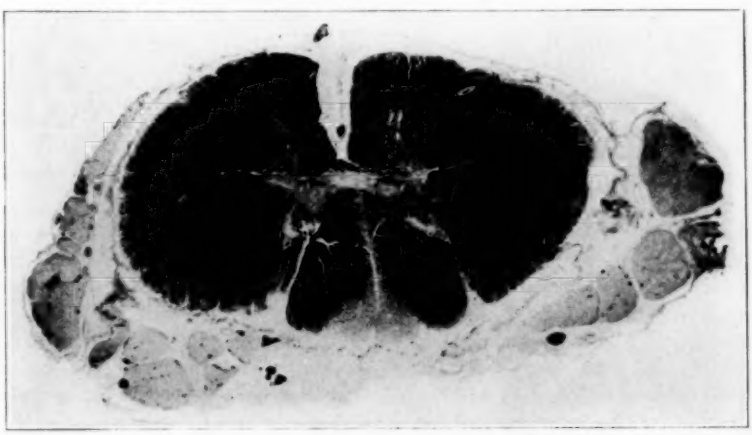

Fig. 2.—Section of the cord from the mid-dorsal region.

power was present in the muscles of the legs, but was practically absent in those of the feet. The thighs were flexed on the abdomen and the legs on the thighs; the knees were ankylosed in a state of semi-flexion, and the feet were in the position of talipes cavus with slight varus. Atrophy and fibrillary twitchings were present in the muscles of the legs, especially in the peroneal and anterior tibial muscles. The patellar and achilles reflexes were absent and plantar stimulation produced flexion on both sides. Incontinence of urine was present, possibly in part due to the patient's mental condition, and in

Fig. 3.—Section of the first dorsal segment of the cord.

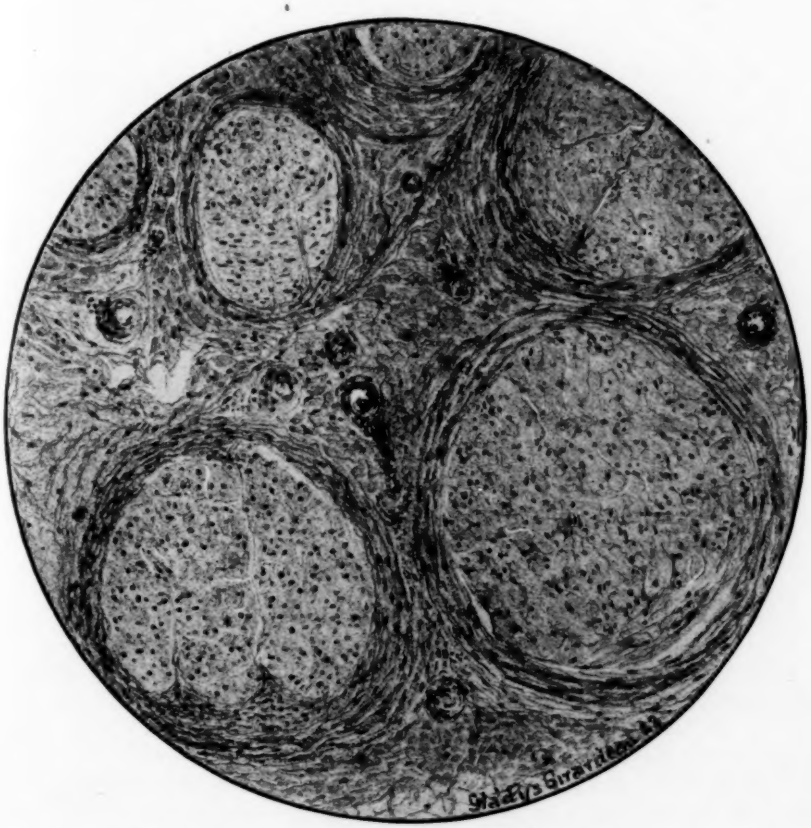

Fig. 4.—Low power drawing of the ulnar nerve.

part to lack of team work between the patient and the attendants. She apparently perceived painful stimuli but other forms of sensation could not be tested owing to lack of cooperation. None of the muscles of the legs, forearms and hands reacted to the faradic current. The Wassermann reaction with both blood and spinal fluid was negative, and no cells were found in the fluid. The patient died May 24, 1920, as the result of broncho-pneumonia.

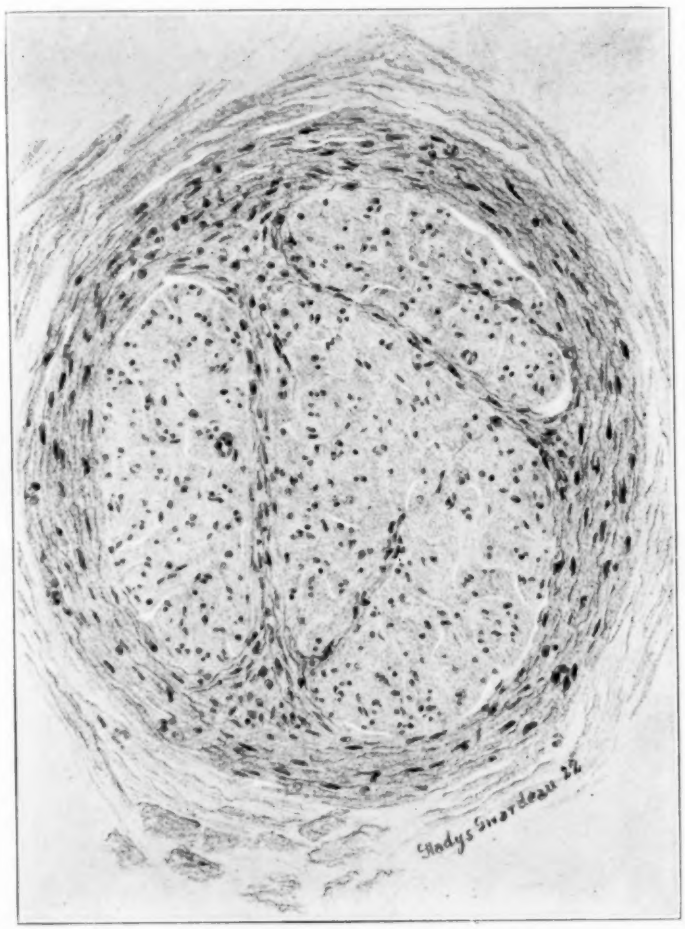

Fig. 5.—High power drawing of the ulnar nerve.

Pathologic Study of the Nervous System.—The spinal cord and the posterior and anterior roots appeared small on gross examination. The meninges, the cells of Clark's columns, and the pyramidal tracts were normal. The anterior horn cells in the lumbar, sacral and cervical regions were diminished in size and number; the nuclei were eccentric, the cell bodies stained poorly and consisted chiefly of a granular material. The changes in the anterior horn cells were most marked in those segments concerned with the muscles of the feet, legs, hands and forearms. In the upper cervical and upper lumbar regions the

cells of the anterior horns were altered but not so severely as those already described. The posterior columns were moderately degenerated throughout all regions of the cord. The degeneration was usually confined to the region about the posterior septum, but in the cervical levels, Burdach's columns were also involved. Lissauer's zones were greatly sclerosed in the sacral, lumbar and cervical regions. The cerebrum showed no changes of note.

The plantar, peroneal, median and ulnar nerves were degenerated, the plantar and peroneal nerves being intensely involved. The plantar nerves contained few healthy fibers; the median and ulnar showed a reduction in the number of healthy fibers but not to the severe degree observed in the plantar and peroneal nerves. The perineurium was greatly thickened in all the nerves examined; the epineurium showed slight hypertrophy, and the endoneurium was not appreciably altered.

Tissue removed from the plantar surface of the foot, and from the thenar and hypothenar eminences showed practically no muscle tissue at all; fat and connective tissue were the only structures present.

COMMENT

The pathologic changes in our case therefore corresponded with the two findings most commonly reported in cases of Charcot-Marie atrophy in which necropsies have been recorded: degeneration of the peripheral nerves and of the posterior columns of the cord. The cells of the anterior horns were more involved in this case than in the one reported by Wilson in 1918.

Clinically, our case showed the presence of mental changes and Argyll-Robertson pupils; these have occasionally been observed in other cases of peroneal muscular atrophy. Indeed, a number of cases have been reported with such atypical manifestations as increased reflexes, Babinski's sign, optic atrophy, ocular palsies and bulbar symptoms. The occasional appearance of these unusual symptoms in Charcot-Marie atrophy may be explained on the ground that hereditary diseases of the nervous system are, at times, blended together; hence atypical findings are to be expected.

RECENT DEVELOPMENTS IN ELECTRODIAGNOSIS*

PERCIVAL BAILEY, M.D., PH.D.
(Ancien Assistant Etranger à l'Hospice de la Salpêtrière, Service du Prof. Pierre Marie.)
BOSTON

It has long been known that in various pathologic conditions the electrical excitability of nerves and the muscles innervated by them is greatly altered. Methods have also been devised by means of which variations in the excitability of these organs may be estimated. They have not, however, come into very general use in the United States.

One of the reasons for the relative neglect of electricity as a diagnostic aid in this country has undoubtedly been the recent astonishing development of the semiology of the nervous system, which has given us a vast number of objective signs and symptoms of derangement of function in various locations. Another reason was the lack of accuracy of the electrical measurements. With the faradic current, the distance of separation of the coils of the inductor may give a fair estimate of the electromotive force developed, but no measure of the time is possible, and the exciting force varies greatly with the physical characteristics of the apparatus and the resistance of the tissues. Even with the simple galvanic current, the size of the electrodes, their position, etc., cause great variation in the findings.

As a result of the inaccuracy of the electrical determinations and the greater ease with which equally valuable information could be obtained by simple clinical examination, there was a tendency for clinicians to ignore electrodiagnosis. Recently, however, particularly in France, great progress has been made in the development of accurate methods, so that today one may determine the functional condition of a nerve or muscle in terms of its electrical excitability with a mathematical precision which objective clinical examination cannot hope to attain. With the exception of the brilliant researches of Keith Lucas,[1] this progress has been made almost solely by the electrophysiologists of France.

The sole contribution to the subject, at least from the clinical point of view, in this country is the recent and interesting work of Sachs and Malone.[2] Certain views supplementary to those exposed in their

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* Reported at a meeting of the Boston Society of Psychiatry and Neurology, Oct. 19, 1922.

1. Lucas, Keith: J. Physiol. **37**:460, 1908.

2. Sachs, Ernest, and Malone, Julian Y.: A More Accurate Clinical Method of Diagnosis of Peripheral Nerve Lesions and of Determining the Early Recovery of a Degenerated Nerve With Report of Cases and Experimental Data, Arch. Neurol. & Psychiat. **7**:58 (Jan.) 1922.

work have seemed to me to need further consideration, particularly in view of recent French work on the subject. In their article, the condenser methods are dismissed as inaccurate. In this view they followed Adrian, who seems to have based his objections mainly on the work of Laugier. Since then, the condenser method has been greatly developed; and the new system found to give accurate results by Laugier [3] himself. It is for this reason that I have thought it interesting to bring these recent developments to the attention of the English reading public. In order to understand the discussion which follows, and to appreciate the merits of the different methods to be described, it is necessary to keep in mind certain fundamental conceptions of current electricity.

ELECTRICAL WAVES USED IN ELECTRODIAGNOSIS

The simplest of all conditions in electrodiagnosis is obtained by the use of the galvanic current. One has to do with the current of constant intensity furnished by a battery of accumulators, which can be closed or opened by means of a hand key. At the moment of closing the circuit the current is established instantaneously, and the intensity rises instantaneously from O to the value determined by Ohm's law $I = \frac{V}{R}$ in which I represents the intensity of the current in ampères, V the difference in potential in volts, and R the resistance in ohms. The current then passes with a constant intensity until the circuit is opened. At the moment of opening, the intensity falls instantaneously to O. The time between the closing and opening of the circuit, during which the current passes, is spoken of as the time, and the portion of current corresponding is known as an electrical wave.

Such a wave may be represented graphically by a rectangle. The quantity of electricity in such a wave is easily calculated, the quantity being the product of the intensity by the time of passage, $q = it$. If in addition to the intensity we know the voltage V under which the current has passed, we can easily calculate the energy furnished, W, by the wave of electricity, the energy being equal to the voltage multiplied by the quantity (when the current is of constant intensity): $W = QV$. If we substitute for Q its equal IT and for V its equal RI, we may write $W = RI \times IT = RI^2T$.

Another type of electrical waves is much used in electrodiagnosis; that furnished by discharge of condensers. The condenser furnishes a wave which attains its maximum intensity instantaneously at the moment of discharge and falls away rapidly to O. It is much more difficult to calculate the quantity of electricity and the energy given by these waves but by means of the integral and differential calculus it may be done, since each has a known logarithmic formula: $I = \frac{V}{R} e^{-\frac{t}{CR}}$.

3. Bourguignon and Laugier: Compt. rend. Soc. de biol., March 5, 1921.

LAWS OF EXCITABILITY

Between 1845 and 1849, Dubois-Reymond,[4] starting from the fact that the closing or opening of a current furnished by an induction apparatus or by a battery of accumulators caused excitation of a nerve included in the circuit, as evidenced by the contraction of the muscle which it innervated, established the famous laws of excitability which bear his name. Without going into their development, since they are familiar to every one, we may enumerate them as follows: 1. The excitation is produced solely by the variation in intensity of the current and not by the absolute value of the intensity. 2. The variation in intensity is the more effective, the more rapidly it is produced. 3. The time of passage of the current and consequently the quantity of electricity and the energy are of no importance in the process of excitation.

The application of these laws to the clinic is the classical search for the minimum intensity which will just give a contraction of the muscle in question when the galvanic current is closed with a hand key, the so-called threshold of excitability.

The laws of Dubois-Reymond have been confirmed for the times of current which he had at his command, but it will be noted that he was limited to the rapidity with which he could close and open the circuit with the hand. In 1864, Fick showed that for still shorter electrical waves, the time factor was of great importance in the process of excitation. Because of technical objections to his apparatus, his results were not generally accepted until Hoorweg[5] in 1897, by the use of condenser discharges, finally proved that for waves of very short duration, the law of Dubois-Reymond was not valid.

LAW OF WEISS

It was not, however, until 1901 that Weiss[6] determined accurately the rôle which the time of passage of the current plays in the process of excitation. He used a constant current, closed and opened by means of a pistol ball. The pistol was so arranged that, when fired, the ball would cut two wires; the cutting of the first wire closed the current, the cutting of the second opened it. The duration of passage of the current was easily calculated from the distance which separated the wires and the known speed of the ball. By means of this arrangement, he showed that the intensity which gives the threshold of excitation diminishes when one increases the duration of passage of the current, until a certain minimum of intensity is reached, when the threshold no longer changes no matter how much one increases the duration.

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4. Dubois-Reymond: Untersuch. über thier. Electr. **1**:258, 1848.
5. Hoorweg: Arch. de physiol., 1897, p. 269.
6. Weiss: Arch. italiennes de biol. **35**:413, 1901.

In representing these results graphically, the times as abscissae and the intensities giving the threshold as ordinates, Weiss established a curve of hyperbolic form (Fig. 1); from a certain duration of current the intensity no longer varies, the hyperbola therefore continues as a straight line. It was this straight section of the hyperbola with which Dubois-Reymond was experimenting. To this hyperbola of intensity corresponds a rectilinear of quantity. The relations of the intensity and quantity of electricity with the time of passage of current constitute

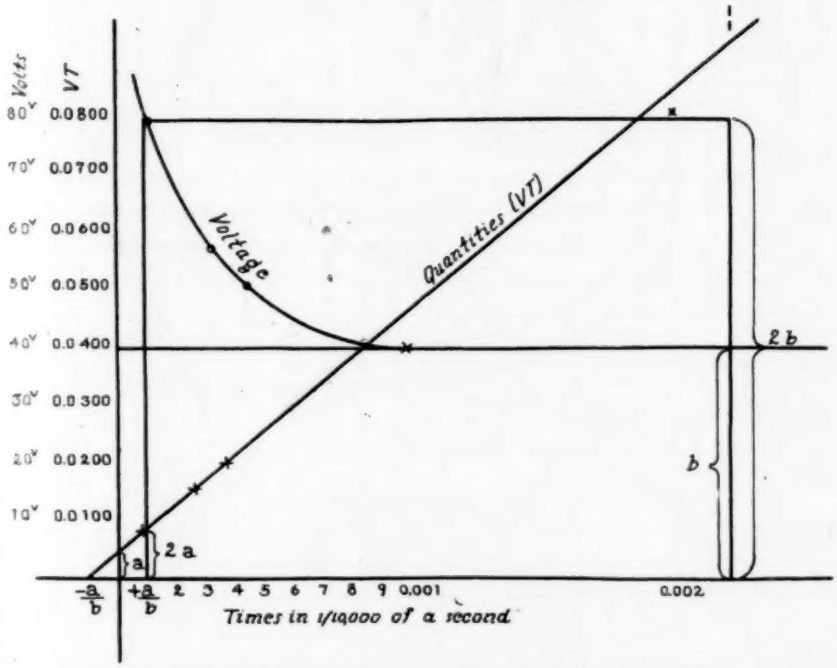

Fig. 1.—Law of Weiss. Right biceps (motor point). $a = 0{,}0035$. $b = 39.^{v}$ $\tau = \frac{a}{b} = 0^{s}{,}00009$ (after Bourguignon).

the law of Weiss, which is general for all tissues excitable by the electric current. These relations may be expressed by the following equations:

$$q = it = a + bt,$$

$$i = \frac{a}{t} + b,$$

in which t represents the time of passage of the current, i the intensity which has given the threshold with the time t, and a and b two constants, of which a is a constant of quantity in coulombs (the quantity which would be sufficient if the wave were infinitely short) and b a constant of intensity in ampères (the minimum of intensity after which the time no longer enters into consideration).

The constant b is familiar and easily determined. It is the galvanic threshold, called by Lapicque the rheobase. The constant a is not directly measurable since it is impossible to employ a current of infinite shortness. It may be obtained by projecting the rectilinear of quantity across the line of infinite shortness of current (Fig. 1, a), or by calculation.

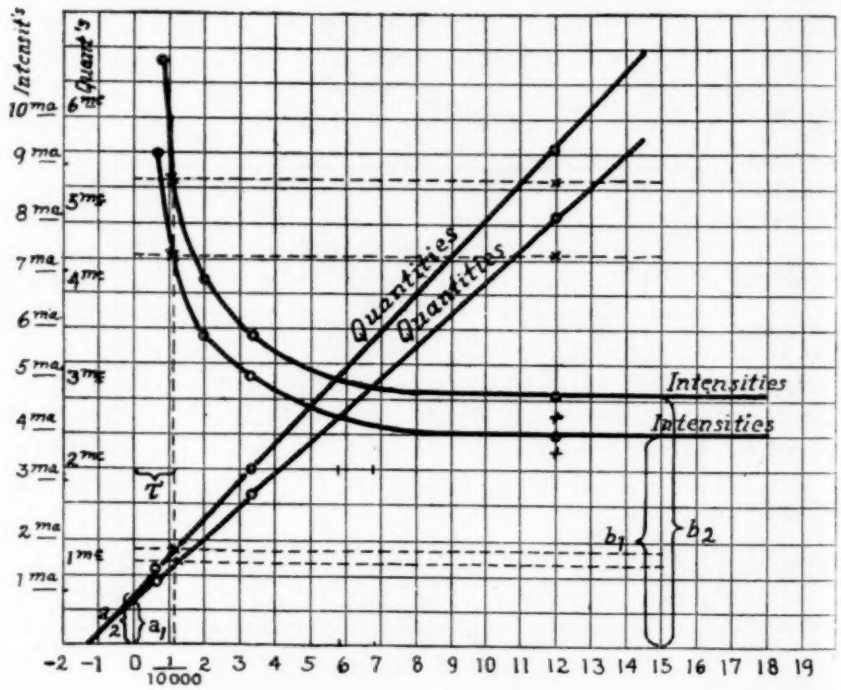

Fig. 2.—Two laws of Weiss obtained from the same muscle with two different positions of the active electrode—left supinator longus; man. Time in 0.0001 of a second. X, points determined experimentally. O, points calculated. $a_1 = 0,^{mc}444$. $a_2 = 0,^{mc}527$. $b_1 = 3,^{ma}7$. $b_2 = 4,^{ma}39$. $\tau = \frac{a_1}{b_1} = \frac{a_2}{b_2} = 0,^{s}00012$ (after Bourguignon).

The galvanic threshold b is therefore not sufficient to characterize the excitability of a tissue. Weiss also showed that while the value of a and b changed with the conditions of the experiment, the ratio $\frac{a}{b}$ of the two constants was invariable, and depended only on the excitability of the tissue examined. He, therefore, suggested that it was in the measure of this relation $\frac{a}{b}$ that one must seek for the characteristic of excitability of nerves and muscles, diseased and well. This relation $\frac{a}{b}$ was named by Lapicque chronaxie, by which it is generally known. Being the product of a quantity by an intensity it is necessarily time in

seconds. Attempts have been made to express chronaxie in terms more accurate than those given in the formula of Weiss, but no one has succeeded in giving an equation at once so simple and so fruitful of results.

Weiss used rectangular waves in his determinations of chronaxie, but any type of electrical wave may be used, for example, the waves produced by condenser discharges. The results, however, will be in terms of the capacity of the condenser instead of time in seconds, and the calculation involved is complicated.

When one uses the current produced by the discharge of condensers, the quantity effective in producing the contraction is not the entire quantity of the discharge, for the tail of the discharge is inactive from the moment when the intensity has fallen below the rheobase. The quantity active Q, which corresponds to the formula $Q = a + bt$ is the quantity exerting its influence in the time between the initial moment of discharge (the potential at this moment may be designated V_o) and the moment when the voltage has fallen to the rheobasic voltage (V_{rh}). By having recourse to the logarithmic formula of the condenser discharge, Cluzet [7] has shown that this time may be expressed $t = RC \log_e \frac{Vo}{Vrh}$. By substituting in the formula of Weiss:

$$Q \text{ or } C(V_o - V_{rh}) = a + bRC \log_e \frac{V_o}{V_{rh}},$$

in which C is the capacity of the condenser in farads, V_o the initial voltage of the discharge in volts, V_{rh} the rheobasic voltage in volts and R the resistance of the circuit in ohms.

From this may be derived the value of $\frac{a}{b}$ in terms all measurable:

$$\frac{a}{b} = RC \left[\frac{V_{rh}}{V_o} - \log_e \frac{V_{rh}}{V_o} - 1 \right]$$

in which R is the measured resistance of the circuit, C is the capacity of the condenser known in advance, V_o is the voltage of charge measured by a voltmeter and V_{rh} the rheobasic voltage measured by the same voltmeter using a constant current. If, now, we assign to V_o a value always the same, say the double of V_{rh}, the formula is simplified greatly and becomes:

$$\frac{a}{b} = RC\ (2 - \log_e 2 - 1) = 0.37\ RC.$$

Lapicque [8] determined experimentally what must be the capacity of a condenser capable of just causing an excitation, with a voltage double the rheobasic voltage, of a muscle with a given chronaxie. He found that the value of the chronaxie could be related to the capacity of the

7. Cluzet: Compt. rend. Acad. d. Sc. **137**:670, 1903.

8. Lapicque: Compt. rend. Soc. de biol., May 7, 1910.

condenser by the formula $\frac{a}{b} = 0.37\ RC$. The formula is usually written $\tau = 0.37\ RC\tau$, in which τ is the chronaxie and $C\tau$ the capacity corresponding. The variation of the experimental result from that calculated mathematically is sufficiently small to be within the realm of experimental error.

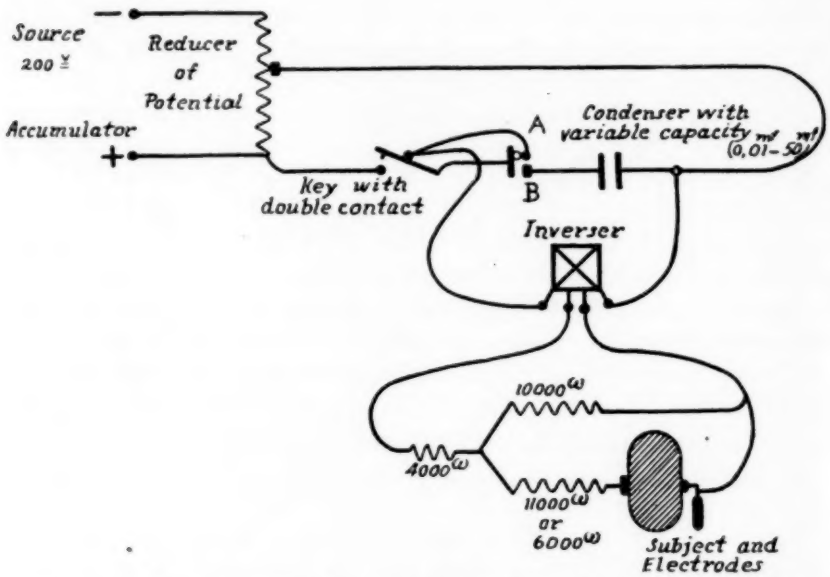

Fig. 3.—Scheme of connections for the determination of the chronaxie on the human subject, by means of the discharge of condensers, after eliminating the variations of the resistance of the subject (after Bourguignon). The connections are so made that with the commutator in the position *A* as represented in the figure, one opens and closes with the key the continuous current; in the position *B*, one charges and discharges the condenser.

THE CHRONAXIE

By a systematic study, Lapicque has shown that the relation $\frac{a}{b}$ is the only constant characteristic of any nerve or muscle, varying in a given tissue only with the temperature. When one makes a series of determinations on a given nerve or muscle, changing each time the experimental conditions, one finds as many hyperbolas of intensity and rectilinears of quantity as there are changes in experimental conditions, but all the hyperbolas are parallel and all the rectilinears converge at the same point: they converge at the point where they cut the axis of abscissae when they are prolonged to the negative side of the axis of ordinates (Fig. 2). There is, therefore, a length of abscissa, that is to say, a time of passage of current, which is constant for a given organ; it is this time which characterizes its excitability and has been called by Lapicque the chronaxie.

Now this point of convergence is exactly where $q = 0$. Since $q = a + bt$, a simple calculation shows that when $q = 0$, $t = -\frac{a}{b}$ we search, on the positive side, the intensity which gives the threshold, when the time of passage is equal to $\frac{a}{b}$, that is to say to the chronaxie, it is easy to see that it is when the intensity is equal to $2\,b$. For, if in the formula of Weiss we take $t = \frac{a}{b}$, the derivative formula $i = \frac{a}{t} + b$ becomes:

$$i = \frac{a}{\frac{a}{b}} + b.$$

Now $\frac{a}{\frac{a}{b}} = \frac{ab}{a} = b$; therefore $i = b + b = 2\,b$.

Lapicque [9] has shown also that, having given the constant b (galvanic threshold) the name of rheobase or fundamental threshold, we may give an empiric definition of the rheobase and the chronaxie independent of all theoretic considerations of the law of excitation:

The rheobase is the intensity necessary to obtain the threshold of excitation on closing a prolonged constant current (the classic galvanic threshold).

The chronaxie is the time of passage of current necessary to obtain the threshold with an intensity double that of the rheobase.

In order, therefore, to determine the chronaxie, it suffices to find the galvanic threshold with the closure of a key, then double the voltage corresponding and determine the time of passage of current necessary to obtain the threshold with a voltage double the rheobasic voltage. For this purpose it is necessary to have at one's disposal a method of obtaining wave lengths in the neighborhood of 0.00001 of a second.

METHODS OF OBTAINING SHORT INTERVALS OF TIME

In order to obtain the minute intervals of current necessary in determining the chronaxie, one may use the pistol of Weiss. This method gives rectangular waves whose length can be measured very accurately. It has been described in the foregoing.

Keith Lucas [1] devised an instrument for this purpose generally known as the Lucas pendulum. It consists of a heavy metal pendulum mounted on a metal wheel in the manner of a hand on a clock. On the rim of the wheel are two keys, the first of which closes the circuit and the second opens it. The pendulum in falling strikes one key after the other. By varying the distance separating the keys any length of time of current may be obtained which is desired, and the time calculated from the known rapidity of falling bodies.

9. Lapicque: Compt. rend. Soc. de biol., July 24, 1909.

A similar instrument, with the wheel mounted horizontally and the hand driven by a falling weight, was devised by Lapicque [10] and called a chronaximètre.

Ströhl [11] has described an apparatus which he calls an égersimètre which replaces most advantageously the pistol of Weiss. A movable weight, moving without friction around a central column, throws the necessary keys, in falling from a height of 18 cm. The interval between the keys is regulated by displacing the movable one on a micrometer scale.

One may also use condenser discharges for the purpose. The time of discharge of a condenser being proportional exclusively to its capacity, it suffices to obtain the capacity which will give the threshold with a voltage double that which has given the threshold with the galvanic current. That capacity may be transformed into time in seconds, that is to say the chronaxie, by means of the formula developed in the foregoing $\tau = RC\,\tau\,0.37$.

APPLICATION TO THE CLINIC

The foregoing work was done, for the most part, on the isolated nerve muscle preparation, but it was promptly realized how valuable it would be could one determine the excitability of the nerves and muscles in the intact human subject, and numerous attempts were made toward this end.

Weiss had already made determinations on the human subject, but his pistol method is too long and tedious ever to come into general use. Adrian [12] has also used the pendulum of Keith Lucas for this purpose, and Ströhl his égersimètre. Lapicque developed his chronaximètre to be used in the clinic. In all of these the keys are a source of continual annoyance, and for this and other reasons they have been abandoned.

In this country Sachs and Malone [2] have described a spring driven instrument resembling the chronaximètre of Lapicque, but in which the troublesome keys have been eliminated. This they have called a chronomyometer. The keys unfortunately have been eliminated at the expense of flexibility, for one is limited, by the construction of the apparatus, to five different times of passage of the current, unless one goes to the trouble of changing the contact plate. Sachs and Malone doubtless never intended it to show more than an approximation of the actual chronaxie, and it serves very well in the gross changes of nerves after section. In many neurologic conditions, however, more accurate

10. Lapicque: Soc. de biol. **78**:695, 1915.
11. Ströhl: Jour. de radiol. et d'electr. **6**:375, 1922.
12. Adrian: Brain **39**:1, 1916.

determinations are necessary. For these it is also necessary to take into account the variations in the resistance of the patient.

Bourguignon [13] has shown that all measures of the resistance of the subject by the aid of the galvanic current were illusory and could not serve for the short waves used in the determination of chronaxie. He was therefore driven to abandon the attempt to estimate the resistance of the subject, without which all measures of chronaxie were erroneous, and succeeded in eliminating it by a method originally devised by Lapicque, as we will show further on.

The sole method of determining chronaxie in the human subject, which, because of its rapidity and accuracy, is actually entering into the daily practice of electrodiagnosis, is the direct outcome of the work of Bourguignon, chief of the laboratory of electrotherapy at the Hospice de la Salpêtrière. Bourguignon [14] makes use of condenser discharges and his method may be described briefly as follows:

The resistance of the patient is eliminated by putting in parallel with him a resistance of 10,000 ohms, the patient and 11,000 ohms in series with him being in the other branch. Four thousand ohms are in series with the system in the general circuit, before the bifurcation (Fig. 3). The circuit thus mounted has a resistance practically constant, no matter what region of the body is examined, its average value being 10,500 ohms. For this resistance it is necessary to use a source of at least 200 volts and nonpolarizable electrodes. It is then only necessary to find the capacity corresponding to the chronaxie and calculate the chronaxie by the formula already given.

With the circuit which Bourguignon uses, one can simplify the calculation, since the resistance is constant. If we express the capacity in microfarads instead of in farads, one microfarad will correspond to a chronaxie of 0^s004, for $\tau = RC\tau \times 0.37$, then $\tau = 1^{mf} \times 10{,}500_w \times 0.37 = 0^s004$. One can therefore simplify the formula of Lapicque and write:

$$\tau = C\tau \times 0^s004.$$

The chronaxie as determined by this method is identical with the figure determined by the pistol of Weiss (when the variation in resistance of the body is similarly eliminated), as I have had occasion to see verified time and again in Bourguignon's laboratory.[3] It evidently gives results coinciding with those obtained by the Lucas pendulum. Adrian [12] gives for the tibialis anticus of the normal human subject, an average chronaxie of 0^s00016. Bourguignon's figure for the same muscle is 0^s00025, sensibly the same for such minute quantities. More-

13. Bourguignon: Acad. d. Sc., Feb. 14, 1916.

14. Bourguignon: Soc. de biol., April 30, 1921; La Médecine **3**: February, 1922; Questions neurologique d'actualité, Masson et Cie. 1922.

over, there is reason to believe Adrian's figure inaccurate, both because of the manner of placing his electrodes, and also because the figure he gives for the nerve of the tibialis anticus is 0.00025. It is known that the chronaxie of a muscle and that of its motor nerve are identical. The method of Bourguignon is, therefore, accurate, and has the great advantage of being very rapid and easy of operation. It enables one to make rapid, accurate determinations and is capable of handling any range of variation of the chronaxie.

The method has one disadvantage; it requires the use of a source of 200 volts. This disadvantage seems to have been overcome in the posthumous work of Guilleminot,[15] who has adapted the method for use on the ordinary 110 volt circuit. He makes use of two condensers, one with a capacity of 0.2 microfarad and the other with a capacity of 20 microfarads. A commutator allows one or the other to be used at will. The resistances are mounted as those of Bourguignon but are only of half the value. The instrumentation is so mounted that also by the use of a special key and manipulator one can make in succession an examination of the faradic excitability, an examination of the galvanic threshold, and finally a determination of the chronaxie with the subject in circuit with the resistances.

The method of operation is based on the formula developed in the foregoing:

$$\frac{a}{b} = RC\left[\frac{V_o}{V_{rh}} - log_e \frac{V_o}{V_{rh}} - 1\right]$$

Using a single condenser, with the resistance fixed, the product RC remains constant and V_o and V_{rh} can be taken as independent variables. One searches the rheobasic voltage by closing the hand key in the continuous circuit, then with the same current charging the single condenser, one searches the threshold of contraction at discharge on augmenting the voltage. The chronaxie may be calculated by the foregoing formula.

To avoid the complicated calculation, Guilleminot makes use of a slide rule, which is so constructed that, since the ratio $\frac{a}{b}$ depends not on the absolute values of V_o and V_{rh} but on the ratio $\frac{V_o}{V_{rh}}$, it reads directly the value of $\frac{a}{b}$ once V_o and V_{rh} are known, provided the product RC is equal to 1. With the system mounted as described the product RC is not 1 but 0.001 with the condenser of small capacity and 0.1 with that of larger capacity. One has, therefore, only to multiply the number read on the slide rule by 1000 or by 10 as the case may be. It is difficult to imagine an easier, more rapid or more effective method. It has been shown by Bourguignon to be sufficiently

15. Guilleminot: J. de radiol. et d'electr. **6**:157, 1922.

accurate for clinical use, and for all ordinary clinical purposes its range is sufficient without surpassing the ordinary voltage of 110 volts.

VALUE OF CHRONAXIC DETERMINATIONS

It will be possible to give only a bare and incomplete outline of the astonishing results of the application of this method in the normal and pathologic human physiology.

Keith Lucas [16] has shown that in the frog's muscle there are three substances with different excitation times which he calls the α, β, and γ substances. The β substance, which in the frog has a characteristic of excitability in the neighborhood of 0.^{s}0001, is doubtless in the human skeletal muscle too rapid to influence ordinary determinations. Adrian [17] was unable to find any evidence of the β substance in the human muscle. The γ substance has been shown to be the nerve fibers and the α substance the muscle fibers.

When its motor nerve is intact, the normal human muscle gives the same chronaxie when excited by the nerve, the motor point or longitudinally. Probably in each case it is the γ substance which is excited. In a pathologic case, however, at the motor point the phenomena are very complex, owing to the fact that the pathologic muscle is heterogeneous and has at least two chronaxies, one smaller by excitation of the nerve and one larger, which is found by longitudinal excitation. In pathologic cases, therefore, the chronaxie should never be determined by stimulation at the motor point.

In pathologic conditions of the peripheral nerves in man, when the muscle is excited by the nerve, the chronaxie rarely surpasses five or six times its normal value; either there are still muscular fibers excitable by the nerve and the chronaxie does not surpass five or six times its normal value, or there are no muscular fibers excitable by the nerve, and the excitation of the nerve is not effective.

There is an intimate relationship between the rapidity and form of contraction and the size of the chronaxie, and in slight pathologic lesions the chronaxie reaches ten to fifteen times its normal value before any slowing of the contraction is visible. The length of the chronaxie varies from 0^s.00008 to 0^s.0007 for a normal muscle, to 0^s.01 to 0^s.07 in the case of a muscle of myotonic contraction.

It is quite evident from the work of Bourguignon, of Adrian and of Sachs and Malone that determinations of the chronaxie enable one to follow accurately the evolution of a pathologic process affecting the neuromuscular mechanism.

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16. Lucas, Keith: J. Physiol. **36**:113, 1907.
17. Adrian: Arch. Radiol. & Electroth. **21**:379, 1916.

Bourguignon [14] has attained astonishing results in his studies of the pathologic physiology. He has shown that the reflex atrophies following joint lesions are accompanied by alteration of the chronaxie of the muscles affected. Every hypertonic or contractured muscle has a chronaxie smaller than normal. Every hypotonic muscle has a chronaxie larger than normal. The attitude of the different segments of the limbs depends on the relation of the chronaxies of the anterior and posterior muscles. In the Parkinsonian syndromes following epidemic encephalitis, for example, with rigidity and bradykinesia, the normal difference between the anterior and posterior muscles of the limbs tends to disappear.

In any segment, the chronaxie is the same for all the muscles which act synergically. Nerves and muscles having the same chronaxies in a limb are attacked or respected by the same morbid agents, for example, in lead poisoning. The flexors háve a chronaxie twice as small as the extensors. The synergic muscles of the proximal segment have a chronaxie from two to five times smaller than those of the distal segment.

For the study of the normal and pathologic physiology of the neuromuscular mechanism, the chronaxie determination has proved its value. Its practical value is not so evident. In traumatic nerve lesions its limitations have been clearly detailed by Adrian.[17] The presence or absence of excitable nerve fibers peripheral to a trauma to a nerve trunk can be detected well enough by the ordinary faradic coil. In the determination of whether the cut end of a nerve is growing down toward the muscle or is blocked by scar tissue, Tinel [18] has shown that there are several important signs of regeneration which appear before there is any change in the electrical reactions. As a rule, incomplete lesions are easily detected by sensory and other neurologic tests. In a few cases the nerve is much less excitable below the lesion than above it, and in this instance the response to short excitations is more readily obtained by stimulating above the site of the injury.

In the case of section or other injury to a nerve, determination of the chronaxie is, however, of value in following the condition of the muscle itself and determining the effect of our efforts to keep the muscle in good condition. In the diagnosis of primary affections of the muscles, such as myopathies and Thomsen's disease, the chronaxie may be found ten to fifteen times its normal value before any slowing of the contraction of the muscle is visible.

Because of the fundamental importance of the work of Bourguignon and his extensive experience, it seems fitting to close with an appreciation of the value of the method in his own words:

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18. Tinel: Les blessures des nerfs, Masson et Cie., Paris.

From a practical point of view the chronaxie gives us a precise measure of the functional value of the nerves and muscles. It permits us to follow very closely the evolution of pathologic processes. It permits us to judge of the efficiency of our therapeutic measures. If it adds little to diagnosis, it is indispensable for the prognosis, to judge the evolution, and to determine with precision the therapeutic indications.

ARSPHENAMIN THERAPY IN STATE HOSPITALS FOR MENTAL DISORDERS *

GEORGE W. MILLS, M.D.
Director of Clinical Psychiatry
AND
CHARLES L. VAUX, M.D.
Senior Assistant Physician, Central Islip State Hospital
CENTRAL ISLIP, N. Y.

The treatment of syphilis in its varied manifestations as encountered in hospitals for the insane is a subject which has interested many physicians, not only those in our own specialty, but also many primarily devoted to other branches of medicine. This, of course, is indicative of its importance, and no one can gainsay the fact that it is a problem of the first magnitude. One finds the most widely diverging views as to the proper method of therapy, as well as to the kind of cases that should be treated, the scale running all the way from the enthusiast who is curing general paralysis, to those who see little or no good in any treatment. This is especially true in instances in which a patient has shown mental symptoms necessitating commitment to a state hospital.

We shall review briefly the literature, outline the plan which has been followed at Central Islip for the past year or so, present our results and our failures, and suggest for consideration a few conclusions.

PART I. REVIEW OF THE LITERATURE

The review of literature which we have made is much too long to be given in its entirety in this discussion. We have summarized this and present it for consideration under nine headings.

1. ARSENIC PENETRATION OF THE NERVOUS SYSTEM

Corbus and others [1] mention experimental work showing that the intravenous injection of hypertonic saline solution (15 per cent.) causes a rapid withdrawal of fluid from the brain. The restoration of fluid begins in about six hours; so they injected arsphenamin intravenously six hours after the salt solution. They believe that the amount of arsenic recoverable from the spinal fluid in their cases was as great as

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* Read at the Interhospital Conferences of the New York Hospitals, Hudson River State Hospital, Poughkeepsie, March 16, 1922, and Utica State Hospital, March 23, 1922, before the Brooklyn Neurological Society, May 17, 1922.

1. Corbus, B. C.; O'Conor, V. J.; Lincoln, Mary C., and Gardner, Stella M.: Spinal Drainage Without Lumbar Puncture; A New Method for Increasing the Penetration of Arsenic Into the Spinal Fluid in the Treatment of Neural Syphilis, J. A. M. A. **78**:264 (Jan. 28) 1922.

with any method suggested to the present time. Mehrtens and MacArthur [2] recovered arsenic in 43 per cent. of their patients treated intravenously; spinal drainage did not increase the number of penetrations, but if meningeal irritation was produced six hours before the intravenous treatment by the injection of a small amount of the patient's serum, the percentage rose to 92, and more arsenic was also recovered. This seems to us to have a bearing on results claimed for the Swift-Ellis treatment. We suggest that this method be tried out by anyone who has faith in the curability of late neurosyphilis with the present arsenic preparations. Morse [3] believes that there is no reliable method for the quantitative estimation of arsenic in such small quantities. He prefers to discuss the matter in terms of concentration, and believes that if the rate of excretion from the central nervous system is equal to that from other tissues, one would expect at the end of a week to have a concentration of at least 1 : 800,000, still probably well within the lethal requirements. Therefore, in giving a course of treatment, the intervals between arsphenamin injections should not be longer than one week.

2. METHODS

From 1917 to 1919, Fordyce [4] and Sachs [5] carried on a wordy war in the medical journals with the intraspinal method pitted against the intravenous. Sachs condemned the intraspinal method, and in a personal communication received in January, 1922, he writes, "I am more opposed to intraspinous therapy than ever I was. I am perfectly frank to state that the intraspinous method has been exploited not always for purely scientific ends, and the dangers of it have never been honestly brought to the notice of the medical public." Kaliski and Strauss,[6] who are associated with Sachs, agree with him in their papers published in 1918 and 1922. Fordyce,[7] on the other hand, continues to be an ardent

2. Mehrtens, H. G., and MacArthur, C. G: Therapy of Neurosyphilis Judged by Arsenic Penetration of the Meninges, Arch. Neurol. & Psychiat. **2**: 369 (Oct.) 1919.

3. Morse, Stern: Personal communication.

4. Fordyce, J. A.: Truth About Intraspinal Injections in Treatment of Spinal Syphilis—A Reply, J. A. M. A. **69**:1482 (Nov. 3) 1917.

5. Sachs, B.: The Truth About Intraspinal Injections in Syphilis of the Nervous System, J. A. M. A. **69**:681 (Sept. 1) 1917. On the Intravenous, Not the Intraspinal, Use of Arsphenamin in Syphilis of the Nervous System, Arch. Neurol. & Psychiat. **1**:277 (March) 1919.

6. Kaliski, D. J., and Strauss, I.: On Syphilis of the Nervous System, Am. J. Syphilis **2**:609 (Oct.) 1918. The Significance of Biologic Reactions in Syphilis of the Nervous System, with Notes on Treatment, Especially Intraspinal, Arch. Neurol. & Psychiat. **7**:78 (Jan.) 1922.

7. Fordyce, J. A.: The Importance of Recognizing and Treating Neurosyphilis in the Early Period of the Infection, Am. J. Med. Sc. **161**:313 (March) 1921.

advocate of the Swift-Ellis method. Solomon [8] agrees with Fordyce and advocates also intraventricular injections when results are not obtained in other ways. Dercum,[9] on the other hand, supports Sachs, and adds that the beneficial effects hitherto ascribed to the Swift-Ellis and kindred methods, are entirely due to the incidental spinal drainage. Dercum's ideas are supported by Schaller and Mehrtens.[10] Stokes and Osborne,[11] who tried out the intraspinal method in a faithful manner, say that they are not convinced that it is of any value. Chargin [12] tried out different dosages and combinations with mercury in active systemic cases; he advocates what he calls a chronic intermittent method, that is, with the arsphenamin injections five days to a week apart, and a course to consist of six to eight injections of arsphenamin, and ten to twelve injections of mercury. His ultimate results were as good as with the more intensive methods, and the toxic dangers were avoided. It seems to be the consensus of opinion that in neurosyphilis moderate doses with reasonable intervals are safest. We think the experience of others justifies us in the plan we have followed at Central Islip.

3. ARSPHENAMIN OR NEOARSPHENAMIN

Rosanoff [13] summarized the opinions of a large number of people with whom he corresponded, and stated that the majority favored neoarsphenamin. Our review also shows that this is the general trend; and the majority of the New York State Hospitals now use the newer product. This preference seems to have a sound physiologic basis, Schamberg [14] stating that while neo-arsphenamin is less active, the discrepancy can be made up by the size of the tolerated dose, and that it is less toxic and causes less biochemical disturbance of the blood and tissues. The time required for administration is, of course, an important point, especially in state hospitals. We recommend that when an arsenical is considered indicated in state hospital work, neo-arsphenamin

8. Solomon, H. C.: Clinic on the Diagnosis and Treatment of Neurosyphilis, Boston M. & S. J. **183**:723 (Dec. 23) 1920; ibid. **183**:768 (Dec. 30) 1920.

9. Dercum, F. X.: The Functions of the Cerebrospinal Fluid, with a Special Consideration of Spinal Drainage and of Intraspinal Injections of Arsphenamized Serum, Arch. Neurol. & Psychiat. **3**:230 (March) 1920.

10. Schaller, W. F., and Mehrtens, H. G.: Therapy in Neurosyphilis with Particular Reference to Intraspinal Therapy, Arch. Neurol. & Psychiat. **7**:89 (Jan.) 1922.

11. Stokes, J. H., and Osborne, E. D.: Relative Effectiveness of Various Forms of Treatment in Neurosyphilis, J. A. M. A. **76**:708 (March 12) 1921.

12. Chargin, L.: Antisyphilitic Therapy, J. A. M. A. **76**:1154 (April 23) 1921.

13. Rosanoff, A. J.: Some Practical Points in the Organization of Treatment of Syphilis in a State Hospital, State Hosp. Quart. **6**:319 (May) 1921.

14. Schamberg, J. F.: Arsphenamin Versus Neo-Arsphenamin, J. A. M. A. **73**:1883 (Dec. 20) 1919.

be used. We feel, however, that there is need of a drug more toxic to the spirochete and less so to the patient, also one which will penetrate better into the central nervous system.[15]

4. PERIOD OF INFECTION OF CENTRAL NERVOUS SYSTEM AND ITS THERAPEUTIC SIGNIFICANCE

Fordyce [7] firmly believes that the involvement of the nervous system occurs during the period of general dissemination or not at all. In his first paper he stated that in the first year following infection the spinal fluid showed evidences of disease in 25 to 30 per cent. of cases, and in a recent paper he and Rosen [16] stated that their figure has risen to 38 per cent. However, they admit that their material is somewhat selected. The 1922 paper of Kaliski and Strauss [6] summarizes the literature bearing on this question, and we think tends to support Fordyce's conclusions, although Kaliski and Strauss themselves believe that a mere increase in cells and globulin with a transient Wassermann reaction, points only to a pia-arachnoid irritation, and that this is, as a rule, temporary and of doubtful significance. Herrick and Dannenberg [17] worked with infectious diseases not syphilitic, and found cells and globulin increased in patients with so-called meningismus. Ravaut [18] believes the early changes are transitory and in the nature of a septicemia. Additional evidence in favor of the belief in the early invasion has

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15. Since this paper was written we have received a circular letter from the New York State Department of Health, recommending arsphenamin in preference to neo-arsphenamin. This letter quotes from a circular letter issued by the Surgeon-General of the United States Public Health Service under the date of April 26, said letter being an order to the medical officers of the Public Health Service and stating, "Your attention is called to the fact that neo-arsphenamine is a much less constant and less reliable preparation than arsphenamine. Not only do certain batches of all brands of neo-arsphenamine show a tendency to deteriorate with age, frequently with definite increase of toxicity, but there is a pronounced irregularity in the therapeutic activity of different batches of neo-arsphenamine, regardless of the source of the preparation. This variation may reach several hundred per cent., and as a result the physician may get a much less satisfactory therapeutic result than when arsphenamine is used, as the latter, regardless of brand or lot number, shows a more uniform therapeutic activity.

"These facts warrant the Bureau in urging that arsphenamine be given the preference over neo-arsphenamine wherever it is possible to administer the former. This choice should be made regardless of mere convenience of administration, in which respect neo-arsphenamine has the advantage."

16. Fordyce, J. A., and Rosen, I.: Laboratory Findings in Early and Late Syphilis, J. A. M. A. **77**:1696 (Nov. 26) 1921.

17. Herrick, W. W., and Dannenberg, A. M.: Observations on the Cerebrospinal Fluid in Acute Disease, J. A. M. A. **73**:1321 (Nov. 1) 1919.

18. Ravaut: Presse méd. **27**:573, 1919.

been quoted by Solomon.[19] The most important point made by Fordyce and others believing as he does is that the time to treat neurosyphilis is in the first year; and it is Fordyce's belief that it will require a long time before these early infections are systematically and properly treated. He lays stress on the improper facilities in public clinics and the lack of routine lumbar punctures.

5. DIAGNOSIS

In discussions on the treatment of neurosyphilis, so-called borderline cases are frequently stressed, and references are made to Dunlap's [20] paper on this subject. There is no question but that the various parenchymatous and mesoblastic changes at times are so equally divided that anatomic classification is difficult or impossible. Nevertheless, Dunlap in his paper states that the groups are ordinarily distinct, and we feel that the cases admitted to state hospitals are, as a rule, clear-cut clinically. The next thing to be considered in making a diagnosis is the serology. Southard and Solomon [21] state that theoretically all tests may be negative and neurosyphilis still be present. It is apparently generally recognized that the spinal fluid may be negative in those cases in which the disease affects almost solely the blood vessels. That entirely negative fluids, that is, negative Wassermann and globulin tests, a normal cell count, etc., occur in other types, seems to us questionable, or at least rare. We did not find reports of any such cases with proper anatomic backing. Published reports of benefits obtained from therapy are frequently invalidated by the number of cases included with primarily negative blood and fluid tests.

6. EVALUATION OF SEROLOGIC CHANGES UNDER TREATMENT

Many workers lay great stress on the serologic changes occurring during arsphenamin therapy. We have seen so many striking fluctuations in the same persons with or without treatment, that we believe extreme caution should be used in weighing them. It is, of course, generally admitted, as stated by Morse,[22] that the Wassermann test is a quantitative relationship between numerous variable factors, both in the specimens and outside of it. Morse thinks that the errors are mostly toward negative results. Of interest in this connection is the case of A. W., who was first admitted to Central Islip in 1916, at the age of 38. Since then he has twice been a patient at this hospital; all attacks have

19. Solomon, H. C.: A Review of Recent Literature on Neurosyphilis, Arch. Neurol. & Psychiat. **7**:235 (Feb.) 1922.

20. Dunlap, C. B.: Anatomical Borderline Between the So-Called Syphilitic and Metasyphilitic Disorders in the Brain and Spinal Cord, Am. J. Insanity, Special Number **69**:1045, 1913.

21. Southard, E. E., and Solomon, H. C.: Neurosyphilis, Boston, W. M. Leonard, 1917.

22. Morse, S.: New York State Psychiat. Bull. **2**:239 (April) 1917.

been of manic-depressive symptomatology, the last following a circular course. He has been at home as long as two years, working efficiently. In 1916, his blood test was reported ++++. In 1917, he is said to have received one intraventricular treatment, one or more intravenous injections of arsphanamin and some mercury. Since then he has received no treatment. His spinal fluid in 1917 is said to have shown 72 cells and a ++++ Wassermann reaction. Recently two punctures have shown 6 cells and the spinal fluid Wassermann test persistently negative. Blood tests, however, have ranged from ++++ to negative; and blood drawn the same day has been reported positive from one laboratory and negative from another. Since 1916, he has shown some pupillary abnormality and unequal knee jerks.

7. LITERATURE FAVORING TREATMENT OF LATE NEUROSYPHILIS, INCLUDING GENERAL PARALYSIS

We reviewed in detail ten or more papers advocating the treatment of paretic patients, but we believe that the authors did not prove their case. Cotton,[23] six years ago, claimed benefit in 58 per cent. of his cases, more than half of which he said had been definitely arrested. One of us recently visited the Trenton State Hospital and found that Dr. Cotton is now only slightly interested in the treatment of neurosyphilis. Solomon,[8] in his earlier writings, makes such statements as, "Every paretic, except those in an advanced stage, should be treated." However, in his latest publication,[24] his statements are much more guarded. Campbell[25] refers to the fact that in the past repeated injections of tuberculin or nucleic acid gave rise to claims of success comparable with those now made for arsphenamin therapy. He says, "Although there is considerable difference of opinion it seems established that intensive treatment of general paralysis is of undoubted benefit in a certain number of cases." However, later in his article he adds, "It is important to remember that one is dealing with a serious progressive deterioration of the brain, the permanent arrest of which is very problematical." Amsden,[26] in 1914, was the first to bring the subject in its entirety before the New York State Hospital group. At first, he thought that he was securing good results. In 1918,[27] he reported on thirty-five cases with 48.5 per cent. of remissions, but in a personal communication received in December, 1921, he stated, "During the last five years we have not

23. Cotton, H. A.: The Treatment of Paresis and Tabes by Salvarsanized Serum, Am. J. Insan. **72**:485, 1916.

24. Solomon, H. C.: A Review of Recent Literature on Neurosyphilis, Arch. Neurol. & Psychiat. **7**:235 (Feb.) 1922.

25. Campbell, C. M., in Nelson's Loose Leaf Medicine, Thomas Nelson & Sons, 1920.

26. Amsden, G. S.: New York State Hosp. Bull. **7**:538, 1914.

27. Amsden, G. S.: New York State Hosp. Quart. **3**:334, 1918.

been doing any intraspinous treatment of paresis in any aggressive way." He thinks that the remissions obtained are somewhat more frequent, somewhat more prolonged and possibly of better character.

8. ADVISABILITY OF TREATMENT IN LATE NEUROSYPHILIS DOUBTFUL

Mitchell [10] of Warren, Pa., in a discussion stated that they had been treating about fifty paretic patients annually for the last ten years, and while they thought they secured a larger percentage of remissions, the majority had been returned to the hospital. As a result of his experience, he regarded any improvement as temporary. Jackson and Pike [28] state that in fifty patients whose condition was diagnosed as parenchymatous neurosyphilis, to whom intensive treatment was given "intravenously, intraspinously and intraventricularly supplemented by mercury and iodides, no lasting results were obtained, and each patient finally succumbed to the disease." Sheehan [29] believes that we are not yet in a position to state the ideal treatment for syphilis. He does not favor the treatment of latent systemic cases, neither do Jackson and Pike. Sheehan considers the prognosis hopeless in paresis and tabes, and that treatment may be contraindicated from a social standpoint.

In our review we found many more in favor of treating late neurosyphilis, including parenchymatous types, than opposed. However, as previously stated, we do not think that therapy as now practiced rests on a sound basis; there seems to us to have been a rush into expensive and intensive wholesale treatment which is not justified by preceding experience with the class of cases admitted to state hospitals.

9. LATENT SYPHILIS

In the literature one constantly encounters the terms "systemic syphilis," "latent syphilis," "neurosyphilis," etc., and we have divided our patients into two groups: those with systemic syphilis and those with neurosyphilis. In the systemic group we placed those with secondary lesions, those with a history of recent infection and those who showed no signs of syphilis except a positive Wassermann test of the blood. We, of course, realize that this division of our material is purely arbitrary. Latency, Wassermann-fastness, etc., are terms with clinical value, but the pathology is not known. Engman [30] states that a continued persistent positive Wassermann reaction usually signifies strains with neurotrophic or vascular affinities. However, we do not

28. Jackson, J. A., and Pike, H. V.: Interpretation of Wassermann Reaction of Blood Serum in Mental Diseases: Indications for Antisyphilitic Therapy, J. A. M. A. **76**:360 (Feb. 5) 1921.

29. Sheehan, R.: Remarks on the Neurology of Syphilis, Mil. Surgeon **49**: 252 (Sept. 21) 1921.

30. Engman, M. F.: Nelson's Loose Leaf Medicine, Thomas Nelson & Sons, 1920.

know where the focus is in our unimproved patients. We cannot say that it is not in the central nervous system; we will hazard no guess as to what later pathologic studies may show in these cases; neither can we assume with Engman that our unimproved systemic patients harbor strains considered resistent. Another alluring speculative possibility is organ inferiority inasmuch as all our patients are insane. Another possibility is infection with a weak or nonvirulent strain, but this entire subject is unknown. Engman and other writers assume that in latent syphilis either changes take place in the pathogenic activity of the organism, or there is an increase in the defensive forces of the cells, and that these changes presumably occur because of the elaboration by the body of immune substances. Just when the production of these stops, its relation to the death of the last spirochete, and the relation of these bodies to the Wassermann reaction, are all speculative questions. It has been stated that a positive Wassermann test indicates that the person is harboring live organisms. They are not always present because they have been demonstrated in a few cases, neither can it be said that the individual does not go on producing antibodies or whatever they are for months or years after all the spirochetes are dead. Eberson,[31] commenting on the finding of spirochetes in semen and lymph glands in cases considered latent, says that because the organisms are found they need not be looked on as evidence of existing disease. Warthin[32] has demonstrated postmortem spirochetes in practically every body organ and tissue of persons who during life gave a negative Wassermann reaction. He says that these organisms morphologically intact may rest there inactive indefinitely; and the fact that in other cases they cause something which gives a positive Wassermann reaction does not prove that they will ever be active in any other way. Conversely, the Wassermann-producing substance may not be present in sufficient quantity to give a positive reaction even when the disease is active clinically. All writers in discussing latent syphilis speculate as to the advisability of treatment. Some feel that there is danger of lighting up an old quiescent process, and nearly all of them refer to the person, frequently encountered, whose infection occurred thirty or forty years before, whose blood is ++++, but who has throughout the entire period enjoyed robust health. These cases always raise the problem of strains, virulence of the organism and natural resistive powers of the host; and Engman says that there is no doubt but that certain strains always portend a grave prognosis. Conversely, there may be strains which injure the person little or not at all, and we feel

31. Survey of Literature: Syphilis, Nelson's Loose Leaf Medicine.

32. Warthin, A. S.: The Persistence of Active Lesions and Spirochetes in the Tissues of Clinically Inactive or "Cured" Syphilis, Am. J. M. Sc., 1916, p. 508.

that the treatment of in old asymptomatic cases should always be approached with caution and reservations. Some syphilologists that we have talked with say that they usually discontinue treatment if no results are obtained after three courses. Engman says it is his experience that if a negative Wassermann reaction does not occur after the second course, it is extremely difficult to obtain. Our own cases bear this out, and also shown that serologic improvement tends to occur after the first course of treatment if it occurs at all.

PART II. THERAPY IN NEW YORK STATE HOSPITALS

In 1918, the New York state hospitals for mental disorders were circularized by Cheney, and at that time little treatment was being given. Since then there seems to have been a steady but slow increase in the number of patients treated. We circularized the twelve other civil hospitals inquiring about the number of patients treated during the fiscal year ending June 30, 1920, compared with those treated during 1921: in general, it can be said that there has been a considerable increase in the numbers treated during the last year. Combining the figures for the past two years, we have 543 patients treated more or less intensively intravenously, most of them selected cases of neurosyphilis with a few of systemic involvement. Five hospitals used old arsphenamin during the period under discussion, but two of these five are now using neoarsphenamin. Only one reported using iodids, but all except one used mercury. One hospital is now using spinal drainage. Nearly all report their general impressions in neurosyphilitic cases as serologic improvement common, general physical improvement fairly constant at least for a time, mental improvement questionable. One hospital reports a tendency to change the diagnosis to cerebral syphilis when improvement occurs in a case thought to be general paralysis; this has been mentioned in several articles. In connection with these reports from the various state hospitals, it is of interest to analyze certain figures given us by Dr. Pollock, statistician to the New York State Hospital Commission (Table 1).

These figures show little change in the number of paretic patients admitted during the last twelve years; the maximum number, 913, were admitted in 1918, and the minimum, 719, in 1912, with 827 during the last fiscal year—a gain of seven over 1920. The percentage discharged as improved and much improved is more interesting. The highest percentage, 17.8, was discharged in 1912; the lowest, 8 per cent., in 1917. In 1920, we see a decided improvement in the discharge rate, but it is still short of that of 1912. This, of course, might be interpreted as an expression of the more energetic and generalized treatment given in 1920; but with still more treatment in 1921, and the fact that we would naturally assume that results from treatment in 1920 would

be registered in 1921, we find instead of an increase, a fall to 12.4 per cent. Although some of the hospitals report the general impression that there are more remissions, this impression is not borne out by the figures of Dr. Pollock; and although some report that they tend to change the diagnosis from general paralysis to cerebral syphilis when marked improvement occurs, a study of the figures for cerebral syphilis does not bear this out. The high point of fifty-four in 1920 was equaled

TABLE 1.—GENERAL PARALYSIS IN NEW YORK STATE HOSPITALS

First Admissions		Discharged as Improved and Much Improved	
Year	Totals, Male and Female	Number	Percentage to First Admission
1910	815	108	13.3
1911	758	98	12.9
1912	719	128	17.8
1913	768	105	13.7
1914	774	96	12.4
1915	814	108	13.3
1916*	640	59	9.2
1917	866	69	8.0
1918	913	90	9.9
1919	880	85	9.7
1920	820	127	15.5
1921	827	103	12.4

* Due to change in fiscal year, only 9 month period reported.

CEREBRAL SYPHILIS CASES IN NEW YORK STATE HOSPITALS

First Admissions		Discharged Recovered		Improved and Much Improved		Total Percentage Benefited
Year	Number	Num	Percentage	Number	Percentage	
1919	26	5	19.2	9	34.6	54
1920	54	3	5.5	9	16.6	22
1921	38	4	10.5	13	34.2	45

TOTAL NUMBER OF PATIENTS WITH GENERAL PARALYSIS AND CEREBRAL SYPHILIS DISCHARGED AS BENEFITED (THIRTEEN CIVIL HOSPITALS)

Year	Total First Admission	Total Number Discharged Benefited	Percentage to First Admisison
1919	906	99	10.9
1920	874	139	15.9
1921	865	120	13.8

in 1913, and in 1921 it dropped back to thirty-eight. Combining the figures for general paralysis and cerebral syphilis, we find 10.9 per cent. discharged as benefited in 1919, 15.9 per cent. in 1920, but 13.8 per cent. in 1921, a loss of 2 per cent.

That the long remissions quoted by some authors as attributable to therapy must be received with scepticism, is indicated by another table prepared for us by Dr. Pollock but not included in this communication, which showed the length of time out of the hospital for patients dis-

charged between 1910 and 1915 and later readmitted. The length of time out included time on parole. Two hundred and fifteen have been readmitted. Of these, twenty-five were out less than six months, but sixty-seven were out from six to twelve months, seventy-two from one to two years, twenty-seven from two to three years, nine from three to four years, eight from four to five years, and seven more than five years. The average length of time was a little more than one and a half years. We think that this remission rate as expressed by discharges must be borne in mind when we note that those treating large numbers of patients in active clinics, such as Solomon, report only one or two or three showing very good results, and seem to refrain carefully from giving the total figures of those treated. We also call attention to the fact that these figures are only for patients discharged and later readmitted, and do not include the large number paroled and returned.

PART III. PROCEDURE AT CENTRAL ISLIP HOSPITAL

In January, 1920, the state board of health began supplying us with arsphenamin, which they continued to do for more than a year. Since then we have used the product of the Dermatological Research Laboratory of Philadelphia, which the state board of health said most nearly resembled their own.

Our purpose was to treat: 1. All patients with so-called systemic syphilis, that is, those having a $++$ or more Wassermann reaction of the blood, or clinical symptoms and with negative findings in the spinal fluid and negative neurologic signs. When the Wassermann reaction was only $++$, it was confirmed by a second test before beginning treatment. 2. Those with cases diagnosed as nonparenchymatous cerebral syphilis. 3. Patients with general paralysis were treated only for special reasons, such as (*a*) those thought to have the early or tabetic type with little brain involvement; (*b*) those who had previously received intensive treatment; (*c*) those whose relatives insisted on treatment. The cases selected, then, were those most favorable for treatment, and included only for some special reason cases with a bad prognosis. This is a significant feature of the cases reported and should be borne in mind in examining the results.

The methods to choose from in administering the arsenicals were many, and the opinions as to their value varied widely. It was decided to adopt a simple, well recognized method and to persevere with it until our results or the findings of others should warrant a modification or change. The administration of arsphenamin intravenously and of mercury intramuscularly was the procedure adopted.

The time consumed varied. It depended chiefly on the ease with which a needle was properly inserted into a vein. Matters were expedited by setting up a second infusion apparatus so that two phy-

sicians could work together. Eleven patients was the greatest number treated at one session, and it required an hour and a half or two hours to treat these when things were running smoothly. When difficulties with the veins were encountered, this time might be extended an hour or two. The amount of time consumed by this method, in which each patient receives 150 c.c. of solution, is a great disadvantage when there are a large number of patients to be treated.

No dangerous reactions followed the administration of arsphenamin, except in one case. Milder reactions varied. Some patients showed none at any time, while others were upset only occasionally. In a few cases we believe errors of technic were responsible. While on the table, the only untoward symptoms noted were nausea and vomiting at the completion of a dose. On one occasion, two patients in succession manifested nausea, and it was believed that insufficient alkalinization was responsible. After that we added an excess of alkali, and we had no further disturbances. On one occasion, most of the patients treated had a rise in temperature and complained of gastric distress, the temperature of one patient reaching 105 F. The next morning they all appeared none the worse for their experience. On this occasion it was thought that the water used was not freshly distilled. Several patients developed an inflamed condition of the skin of the arm with exfoliation. A dressing of aluminum acetate, followed in a few days by zinc oxid ointment, usually cleared up the skin. The conditions were evidently due to leaking of the arsenic solution into the tissues around the vein. One patient had considerable induration, and his arm was massaged for several weeks. Another patient who had shown some nausea after each dose of his fourth course, had this inflamed condition at the bends of both elbows. The administration of arsphenamin being continued, he then had numerous patches of exfoliative dermatitis on his body. One patient developed an intense exfoliative dermatitis after his third dose. This began over his ears and spread over his body. His condition became critical. He ran a temperature ranging as high as 105 F. for more than a week. A general furunculosis was superimposed, and he still had large abscesses in the axilla a month later. The condition finally cleared up.

We had considerable difficulty in obtaining a suitable mercury preparation. We experimented with several, and finally adopted the ampules of mercuric salicylate as supplied by any of the wholesale drug firms. We found this suspension entirely satisfactory from both mechanical and physiologic standpoints, the latter as shown by salivation. We found that we could seldom give more than 1 grain weekly for the full course of ten weeks. At times the mercury was given coincident with the arsenic preparation. Again one course followed the other. Scham-

berg,[33] in recommending that the mercury follow the arsenic, says, "Vigorous mercurial treatment is often responsible for arsenical intoxication." Our two patients with exfoliative dermatitis were taking both arsenic and mercury at the time this condition developed.

TREATED SYSTEMIC CASES

The results of treatment may be discussed under four headings:

1. *Wassermann Results* (Table 2).—There were twenty-three cases in this group. The courses given ranged from one to four, each course consisting of five or six doses of arsphenamin and ten doses of mercury. Dividing these cases according to the results of the Wassermann test, we have four groups.

Group A, Negative: This group consists of all cases in which a persistent negative Wassermann reaction was obtained. Nine cases became negative, but in three of these a positive reaction again appeared, leaving six cases in this group. Five of these, Cases 1, 2, 4, 5 and 7 became negative after one course of treatment; one, Case 3, after two courses.

Group B, Reduced: This group consists of all cases in which there was a reduction in the degree of positiveness of the Wassermann test but without a negative reaction. There was a slight reduction in four. Three cases, Cases 6, 14 and 15, were reduced after one course; one, Case 11, after three courses; and in all four the change was only 1 degree.

Group C, Not Reduced: This group consists of some unchanged cases, and of others showing changes in the Wassermann reaction, but without permanent reduction. There were eleven cases in this group. Three cases, Cases 10, 13 and 20, were not reduced after one course; three, Cases 16, 17 and 19, were not reduced after two courses; two, Cases 8 and 9, were not reduced after three courses, and three, Cases 12, 18 and 21, were not reduced after four courses.

Cases 12 and 21 are interesting because the blood became negative after the first course, positive after the second course, and again more positive after the third and fourth courses. As Case 12 had only a + blood test before treatment, one might ask whether a quiescent latent syphilis was not roused to renewed activity by the treatment.

Group D, Died: Two of the patients died within six weeks of the last dose, without tests being made, one of tuberculosis and one of enteritis.

2. *Clinical Improvement Compared with Serologic Results.*—In this group of systemic cases, clinical improvement could in general be

33. Schamberg, J. F.: Clinical Commentary on Studies of Histologic Changes in Organs Induced by Arsphenamins, by Neo-Arsphenamin and by Mercury, Arch. Dermat. & Syph. **3**:571 (April) 1921.

TABLE 2.—SYSTEMIC CASES *

Case	Age	History	Previously Treated	First Test			After 1 Course, Blood	After 2 Courses, Blood	After 3 Courses, Blood	After 4 Courses, Blood	Final Test, Blood	Months Observed	Outcome
				Blood	Spinal Fluid	Cells							
1	30	+	..	++++	..	..	—	.....	.....	.....	—	10	P
2	25	+	+	++	—	Bd	—	.....	.....	.....	—	9	P
3	20	+	—	++++	—	2	++	—	.....	.....	—	16	P
4	42	+	—	+++	—	1	—	.....	.....	.....	—	10	P
5	39	+	+	+++	—	Bd	—	.....	.....	.....	—	18	P
6	43	+	+	++	—	7	+	.....	.....	.....	+	9	P
7	23	—	—	++	—	3	—	.....	.....	.....	—	10	P
8	27	+	+	+++	—	0	+	—	++++	....	++++	11	H
9	36	+	+	++++	—	..	++++	++	++++	.....	++++	17	H
10	21	—	—	++	—	3	++	.....	.....	.....	++	30	P
11	29	—	—	+++	—	7	+++	+++	++	.....	++	20	H
12	41	+	+	+	—	3	—	++	+++	++++	++++	27	H
13	31	—	—	+	—	..	+	.....	.....	.....	+	18	H
14	50	—	—	++++	—	7	+++	.....	.....	.....	+++	15	H
15	46	—	—	+++	—	3	++	.....	.....	.....	++	15	H
16	48	—	—	++++	—	3	++++	++++	.....	.....	++++	19	H
17	34	—	—	++++	—	5	++++	++++	.....	....	++++	8	H
18	27	+	—	++++	—	5	++++	++++	++++	++++	++++	24	H
19	45	+	+	++++	—	2	++++	++++	.....	.....	++++	26	H
20	38	+	+	++++	—	3	++++	.....	.....	.....	++++	10	H
21	45	—	—	+++	—	0	—	+	++	++++	++++	27	H
22	25	+	—	++++	—	1	.....	.....	.....	.....	.....	4	D
23	58	—	—	++++	—	2	.....	.....	.....	.....	.....	3	D

* In this table and in Table 4, + in history column means "history of syphilis obtained"; — means "not obtained." + in previous treatment column means "history of previous treatment"; — means "none." All other + and — signs refer to Wassermann tests. In outcome column: P means parole; H, still in hospital; D, died.

correlated with a reduction in the positive findings in the blood Wassermann test. In other words, as shown in Table 3, patients with a reduction in the degree of positiveness of the Wassermann reaction were more often the ones showing mental or physical improvement or both, or vice versa.

Summarizing these, we find clinical improvement in seven cases out of ten that showed a reduction in the Wassermann test. Four patients improved clinically out of eleven that showed no reduction in the Wassermann test.

3. *Age of Infection Compared with Results of Wassermann Test.*—The effect of treatment in relation to the duration of the disease deserves consideration.

We find that in our cases a reduction in the Wassermann test was more frequent in those of short duration. It occurred in all three cases of less than one year's duration. In cases ranging from three to twenty

TABLE 3.—CASES OF SYSTEMIC SYPHILIS *

Group	Results of Blood Wassermann Test	Mental and Physical Improvement	Mental Improvement Only	Physical Improvement Only	Unimproved	Died	Total
1	Reduced to —	2-4-5-7	.....	3-1	.....	.....	6
2	Reduced.....	.....	.....	11	6-14-15	.....	4
3	Not reduced.....	10	12	13-20	8-9-16-17-18-19-21	.....	11
4	Not tested.....	.....	.....	.....	.....	22-23	2
	Total.....	5	1	5	10	2	23

* Figures in all except totals refer to case numbers.

years' duration, the exact length of time the syphilis had existed seemed to be of little moment, Case 18, of six years' duration, showing no reduction after four courses, and Case 4, of twenty years' duration, maintaining reduction after one course.

4. *Effect of Previous Treatment.*—There was a history of previous treatment in seven cases. The amount of this treatment varied. Most of the patients treated had received mercury and some of them arsphenamin. In none was the treatment considered intensive. Reduction in the Wassermann test was obtained in cases of short duration, but no influence of previous treatment was observed in cases of long duration.

CASES OF TREATED NEUROSYPHILIS

1. *Serologic Findings Following Treatment* (Table 4).—There were fifteen cases in this group. Of nine cases in which both the blood and spinal fluid were retested, two, Cases 1 and 4, showed a decreased Wassermann test in both, with a reduced cell count. One case, Case 12,

TABLE 4.—Cases of Neurosyphilis

Case	Age	History	Previous Treatment	First Test			After One Course			After Two Courses			After Three Courses			Final Test			Months Observed	Outcome
				Blood	Spinal Fluid	Cells	Blood	Spinal Fluid	Cells	Blood	Spinal Fluid	Cells	Blood	Spinal Fluid	Cells	Blood	Spinal Fluid	Cells		
1	30	+	+	++++	++++	50	+	++	16	.....	.....	.....	.....	.....	.....	+	++	16	5	P
2	43	+	—	—	++	10	—	—	11	—	+++	12	—	++++	1	—	++++	1	21	P
3	32	+	+	++	+	65	+++	++++	...	.....	++++	50	.....	.....	.....	.....	++++	50	28	P
4	28	—	+	++++	++++	318	++	+++	124	++	—	26	.....	.....	.....	++	—	26	22	H
5	23	+	—	++++	++++	1	+	.....	.....	.....	.....	.....	.....	.....	.....	+	.....	.....	28	H
6	25	—	+	++++	—	39	++++	.....	.....	.....	.....	.....	.....	.....	.....	++++	.....	.....	15	H
7	31	+	—	++++	++++	76	++++	.....	.....	.....	.....	.....	.....	.....	.....	++++	.....	.....	6	P
8	33	+	—	++	++++	63	++	—	41	++	.....	.....	++++	.....	.....	++++	++++	12	24	H
9	54	—	—	++	—	43	++	—	9	.....	.....	.....	.....	.....	.....	++	—	9	18	H
10	47	—	—	++++	—	2	—	.....	.....	.....	.....	.....	.....	.....	.....	+++	—	0	11	H
11	26	+	+	++	++++	22	—	.....	.....	.....	.....	.....	.....	.....	.....	—	.....	.....	24	D
12	39	+	—	+	++++	196	+++	.....	.....	+	++	14	.....	.....	.....	+	++	14	26	D
13	30	+	+	+	++++	77	—	++++	.....	++++	++++	20	.....	.....	.....	++++	++++	20	16	D
14	50	+	—	++++	++++	.....	+++	.....	.....	.....	.....	.....	.....	.....	.....	+++	.....	.....	15	D
15	37	+	+	±	++++	70	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	13	D

showed a reduction in cells and in the spinal fluid Wassermann test, but no change in the blood. Cases 2, 3, 8, 9, 10 and 13 showed a reduction only in cells. Of five cases retested only in the blood, three, Cases 5, 11 and 14, showed a reduction; in the other two there was no change. None reached and maintained a negative Wassermann test in either the blood or spinal fluid, except one case, Case 11, in which the patient died.

2. *Clinical Improvement Compared with Serologic Findings* (Table 5).—Mental and physical improvement were noted in three cases, Cases 1, 2 and 7. Case 1 showed reduction in the Wassermann test of both the blood and spinal fluid and a reduced cell count after only three doses of arsphenamin and five of mercury. The patient in Case 2 showed no reduction serologically after two courses in the hospital;

TABLE 5.—CASES OF NEUROSYPHILIS *

Group	Serologic Results	Mental and Physical Improvement	Mental Improvement Only	Physical Improvement Only	Unimproved	Died	Total
1	Reduction in blood, spinal fluid and cells	1	.....	.....	4	....	2
2	Reduction of spinal fluid and cells	.....	.....	.....	.....	12	1
3	Reduction of cells only	2	.....	3	8-9-10	13	6
4	Reduction of blood only	.....	.....	.....	5	11-14	3
5	Not reduced	7	.....	.....	6	....	2
6	Not tested	.....	.....	.....	.....	15	1
	Total	3	0	1	6	5	15

* Figures in all except totals refer to case numbers.

he improved clinically and was paroled. He is receiving further treatment in a New York City clinic, and on the last examination outside the hospital, the cells were reduced to 1, while the spinal fluid was + + + + and the blood continued —. In Case 7, the blood was not reduced after one course; the spinal fluid has not yet been reexamined. He is still receiving treatment in the city clinic. Physical improvement alone was noted in Case 3. The patient showed no reduction of positiveness in the blood or spinal fluid after one course of treatment here; he was paroled and received six intramuscular, six intravenous, eight intraspinal and one intraventricular treatment outside. The spinal fluid continued to be + + + +; the last cell count was 50 as compared with 65 before treatment.

3. *No Clinical Improvement and Death of Patient.*—Four patients, Cases 5, 6, 9 and 10, were unimproved after one course of treatment. One of these, Case 5, showed reduction in the Wassermann test of the

blood, and two, Cases 9 and 10, showed a reduction in cells. However, in Case 10 both counts were within the normal limits. One case, Case 6, showed no change.

There was no improvement in Case 4 after two courses of treatment by us. There was a reduction in the cells and in the blood and spinal fluid Wassermann tests. This case is of interest because of previous treatment. The patient had spent two and a half years in another hospital, where he received nine intraventricular injections as well as sixteen intravenous and twelve intraspinal injections. Just prior to his discharge from the other hospital, tests showed only 4 cells, but the globulin test was + and the gold chlorid 5554300000; the Wassermann test was not reported. Under treatment in Central Islip, the cells were reduced from 318 to 26, the spinal fluid from + + + + to — and the blood from + + + + to + +. In view of our findings in all cases, we attach no importance to these changes. The other case, Case 8, was complicated by the presence of a bullet in the temporal fossa. The patient's spinal fluid varied at different times from — to + + + +. The cells were fairly constant for tests made over twelve years, ranging from 40 to 60, and did not change after three courses of treatment until after the removal of the bullet, when they were reduced to 12, both the spinal fluid and blood Wassermann tests at this time being + + + +.

Five patients died; three, Cases 11, 14 and 15, after one course, and two, Cases 12 and 13, after two courses. The patient in Case 12 showed a reduction to + + in the spinal fluid test and a reduction in cells from 196 to 14. In Case 13 both blood and spinal fluid tests were + + + +, with a reduction of cells from 77 to 20. Both patients died within six weeks of the last dose. In Case 11 there was a — Wassermann test in the blood after one course. The patient in Case 15 died without retests, and in Case 14 the blood was reduced only 1 degree, the spinal fluid not being retested.

In this group, then, we find little correlation between the reduction serologically and clinical improvement, a striking contrast when compared with the systemic cases (Tables 3 and 5).

Variability of Findings in Both Groups of Cases.—In most of the cases more tests were made than are recorded in the tables, and frequently a negative or + would appear in cases in which the result was regularly + + + +. This cannot in any way be correlated with the treatment, as it occurred in some cases before treatment, and a positive result might follow a course immediately, to be succeeded by a negative result a few months later, or vice versa, without any uniformity or apparent reason. On this account many patients had more than one Wassermann test made between courses, and at

times findings of another laboratory were used in checking up reports. This held true of the spinal fluid as well as the blood, and cell counts were found to vary within a wide range as well.

PART IV. CONCLUSIONS

1. The division of our case material into systemic and neurosyphilitic is purely arbitrary, but conforms to the present accepted nomenclature. We realize that in our old asymptomatic cases we do not know where the focus of disease or of spirochetes is; in fact, we do not know that there is any disease, or even that there are live organisms.

2. Speculation as to strains, virulence, natural body resistance, Wassermann-fastness, latency, etc., would be premature and has not as yet a sound pathologic and clinical basis.

3. Granting that the foregoing limits the scope of our conclusions, we feel that the literature can be summed up and correlated with our own material, and that certain definite recommendations and impressions can be stated.

4. Arsenic penetration of the central nervous system is said to be much increased by inducing a sterile meningitis and may be the mechanism accounting for the benefits attributed to the Swift-Ellis treatment.

5. We think it is conceded that about one third of all cases of syphilis show changes in the spinal fluid in the early stage of the infection, and that about 10 per cent. develop frank serious involvement of the nervous system.

6. Until there is better treatment of syphilitic patients in the early stages, and until a radical change occurs in the methods followed by metropolitan clinics and physicians in general, we do not look for any material reduction in the number of late cases needing institutional care.

7. We question very much the reliability of reports giving results of treatment in neurosyphilis with primarily entirely negative spinal fluid, and we call particular attention to the general lack of necropsy material. We also question the therapeutic significance of varying degrees of positiveness of the Wassermann reaction, but are not in a position to draw any conclusions along these lines as to the gold chlorid test. We do believe that the gold chlorid test should be performed in all cases.

8. As to methods: We believe that the consensus of opinion is that in systemic cases definite courses of an arsenic preparation and of mercury should be given; that the arsenical should be given in moderate doses and not more than one week apart; that to effect a cure in even early systemic cases prolonged treatment should be given. As to neurosyphilis: We believe that the multiplicity of methods is merely indicative of the seriousness of the disease and impossibility in general of

affecting it favorably. We feel that none of the direct methods so far advanced has solved the problem, and our review of the literature has not convinced us that their advocates have proved their case. We are impressed with the experimental work in inducing meningeal irritation and would like to see more done along this line.

9. Our experience, although in only two cases, bears out Schamberg's statement that the toxicity of the arsenical is increased by giving mercury at the same time. We recommend that it be given as a separate course following the course of arsphenamin.

10. In the so-called latent systemic cases as encountered in state hospitals, unless serologic improvement occurs after the first course, none is to be expected; and if this improvement is only a slight reduction in the degree of positiveness, it is of little significance.

11. In only two of our cases in the systemic group was syphilis thought to have a direct bearing on commitment; nevertheless, clinical improvement could, as a rule, be directly correlated with serologic improvement.

12. Our material shows that when the duration of the systemic syphilis is one year or less, therapeutic response is to be expected; after three years it is much less certain.

13. In our neurosyphilitic group, all patients who were retested showed a reduction in cells. None reached and maintained a negative Wassermann reaction in either the blood or the spinal fluid, except one that died.

14. Five improved sufficiently clinically to warrant parole; however, in only two patients, or 14 per cent., could treatment have been of any influence, which is little better than the remission rate for the entire state.

15. Our neurosyphilitic group does not show the correlation between clinical and serologic changes that the systemic does; two cases closely resembling each other in the period since infection and the nature of the process clinically progressed rapidly to death, although one showed well marked improvement in the blood and spinal fluid findings.

16. Although the literature contains numerous warnings in discussing therapy in the latent cases, we believe that our own material justifies at least one course, which must, however, be carefully given and the effects watched. Each case of this kind must be judged on its own merits with due regard to the age of the patient, general bodily health, past history, nature of the psychosis, etc., and continued treatment governed by results.

17. Although the majority of the authors reviewed favor treatment of neurosyphilis, we feel that nearly all of their reports are open to serious criticism; and many who advocate treatment of the paren-

chymatous types admit their lack of success. It is also to be noted that some of those formerly enthusiastic have greatly receded from their earlier position.

18. As our case material tends to show that prolonged conscientious intravenous treatment does not, as a rule, clear up old latent supposedly systemic syphilis, judging by the blood Wassermann reaction, on theoretical grounds alone, we would feel hopeless as to its efficacy in nervous system involvement. We feel that there is need of a drug more toxic to the spirochete and less so to its host.

19. Although our present material includes only cases in which intravenous therapy was employed, we nevertheless believe that in general, paretic patients should not be treated, at least not those admitted to state hospitals. We also believe that patients suffering from what is designated as late cerebral syphilis should usually not be treated, and that the time to treat neurosyphilis is during the first year or so after the primary infection.

20. We do not believe that the so-called borderline cases should be stressed from a therapeutic standpoint; that, on the contrary, the cases admitted to state hospitals are usually clear-cut clinically.

21. During the last two fiscal years there has been a decided increase in the number of syphilitic patients treated in the New York state hospitals; this has not been reflected in the discharge rate.

22. The economic side has at times been stressed, but we fail to see the economy when at best all that is produced is a remission; and to the expense of drugs must be added the expense of total longer care.

23. We place no reliance on one negative Wassermann reaction in a case under treatment; and, in view of the numerous discrepancies and contradictions which we have seen in the serology, we recommend repeated examinations in all unclear cases, and especially examination in more than one laboratory.

SCHIZOPHRENIC CATATONIA WITH ASSOCIATED METABOLIC AND VEGETATIVE FEATURES*

REPORT OF A CASE

THEOPHILE RAPHAEL, A.M., M.D.

JOHN PURL PARSONS, B.S., M.D.

AND

MARGARET NEWELL WOODWELL, A.B.

ANN ARBOR, MICH.

The case here reported is one of classic catatonic stupor, with marked improvement on continued hospital residence. It was possible to carry out a series of very careful physiologic studies upon this case, and the resultant findings indicate definite deviation in this field; these were particularly marked during the acute phase of the disorder and, in general, appeared to run directly parallel with essential fluctuations in the actual psychiatric status. In view of the attention now directed toward the physiologic substrate in schizophrenic disorder, it was felt that the presentation of such a study of a case which stood out clinically in such striking relief, would prove of interest; especially, since it emphasizes the paramount importance of what may be termed long-section study, in the proper evaluation of such material.

REPORT OF CASE

Clinical History.—F. W., a schoolboy, aged 14, was admitted to the State Psychopathic Hospital Sept. 6, 1921.

The father is an unsuccessful farmer. Both parents are extremely religious, and belonged to the "Crusader" sect prior to marriage; the home atmosphere was, therefore, intensely and narrowly religious. The mother is nervous, high strung and definitely of the zealot type. She has suffered several "breakdowns" which were characterized by irritability, restlessness and hypersthenic trends. The patient's father, who is thirteen years younger than his wife, is of very serious mind but is apparently not nearly so extreme in his views as she, although he had been a pastor in the "Crusader" church before he became a farmer. He gives a history of having had Pott's disease which, of late, seems to have become practically quiescent. For over a year, he has suffered from more or less intractable diarrhea, which is apparently associated with considerable pain and is considered by the family physician to be tuberculous in nature. The patient's older brother is reported to have suffered from tuberculosis of the hip, which is at present inactive. A maternal uncle is said to have experienced a "nervous breakdown" in his youth, while studying in a theological seminary. This continued for a number of months and was character-

* From the State Psychopathic Hospital, Ann Arbor, Mich.

ized by restlessness, ambivalence, and seclusiveness, with autistic trends. He was unable to continue his studies but undertook some evangelical work, in which he is still active. He has had several further "breakdowns" which were somewhat less severe but apparently of the same kind. The family history, as obtained, was otherwise negative.

The patient's birth was normal. He had the usual children's diseases and seems to have been particularly prone to bronchitis and tonsillar disorders. As a child he is described as frail, and very obedient; he never required punishment, was very religiously inclined, not gregarious and not especially fond of outdoor sports. He much preferred to remain at home reading and day-dreaming, a trend which was definitely fostered by the intensely religious and restrictive influences of his home. In school he was an exceptionally bright, assiduous pupil; in spite of interruptions, he completed the tenth grade at 14 and is described by his last teacher as of an extremely mature and receptive intellect.

For two years before admission the patient had been compelled, because of his father's failing health, to help considerably with the farm work. As a result of this he regressed somewhat physically. He had very little leisure time, turned from heavy farm work to study, and at times was forced, for varying periods, to interrupt his school attendance. These facts, added to the stress of attendant poverty seemed to depress and worry him, as he took his schooling with profound seriousness and was ambitious for a university career.

No frankly psychotic change was noted, however, until about a year before admission to the hospital when the patient was observed to have developed a mild, and at first rather undirected, nosophobia, which very soon became characterized by certain definitely psychopathologic trends. For example, he refused to open his mouth any more often or more widely than was absolutely necessary, but, when he did so, he was observed to expectorate vigorously afterward for some minutes. This reaction was found to be dependent upon a fear of admitting disease organisms into the mouth and causing a systemic infection. He became over-scrupulous in personal cleanliness, washed his hands almost incessantly and bathed much more frequently than usual. Following this, the patient began to complain of vague somatic distress, and later insisted that he had contracted appendicitis, in spite of the fact that repeated examinations by local physicians failed to reveal any evidence of such a process. He became progressively more seclusive, and in time seemed to lapse, almost wholly, into a state of autistic concern and reverie. He moved in a stereotyped fashion, assumed constrained postures, and finally became mute, refused to eat, and spent the entire day sitting or lying in stiff postures and staring into space. It is interesting to note that, at about the time of the onset of the mental change, the patient was observed by his father to have developed a definite bradycardia; the pulse rate rarely exceeded 60 and often fell as low as 48.

Clinical Course.—The patient's progress in the hospital was typically that of schizophrenic catatonia, with improvement after some five months of residence. On entry, he showed stereotypy of movement and posture, and lay all day prone upon his bed, with his hands close to his sides, and his gaze directed fixedly to the ceiling; yet he was, apparently, fully alive to the general environmental situation. Whenever he left his bed, he did so in a slow, mannikin-like fashion and, upon returning, went through a certain set, stereotyped routine, particularly as to tucking the bed-clothes under his armpits. He was absolutely mute except in the morning and evening when he would kneel by the

bed and pray in a whisper. He was further negativistic in that he refused to eat or even to open his mouth, and it was necessary to feed him by tube for almost five months. He appeared completely indifferent to painful stimuli and to threats; in short, he presented a typical picture of acute stuporous catatonia.

Examination.—During this phase, except for some degree of general emaciation and asthenia, the patient showed no gross somatic deviation, though there were certain features indicative of the carnivorous body type, or habitus, of Bryant.[1] Of late this has come to be construed as a frequent associate of the clinical vagatonias of Eppinger and Hess. The characteristics were: flat thorax; somewhat long, thin neck; long tapering fingers; cyanotic extremities; low tension pulse, with bradycardia (46 to 58 per minute); hypopiesis (systolic 90 to 100, diastolic 65 to 85); coarse, dry, rather darkly pigmented skin; winged scapulas and visceroptosis. The axillary temperature range during this period was from 96 to 97 F. Roentgenologic study of the skull, thorax and extremities yielded no evidence of endocrinopathic or other pathologic deviation, and examination of the urine and blood were entirely negative.

Neurologic examination disclosed nothing of note except mydriasis and marked dilator dermographia; the latter at times took on a highly specific and localized character; thus, frequently, particularly after physical pain or affective stress, one hand became red, engorged, and actually hot, while the other appeared cyanosed, frigid, and of distinctly lesser size.

Pharmacodynamic studies afforded frank evidence of a vagotonic trend. Pilocarpin, one-eighteenth grain (0.004 gm.), induced very marked sudomotor response; one-quarter milligram of physostigmin caused cardiac slowing, and one-hundredth grain (0.0006 gm.) of atropin produced but slight tachycardia. The oculocardiac reflex, however, was negative. One milligram of epinephrin, given subcutaneously, was practically without effect; the pulse acceleration was consistently less than 10 and the rise of blood pressure was only 2 to 5 mm. The increase in basal metabolic rate which followed the intramuscular administration of 1 mg. of epinephrin, was only + 7 per cent. (average normal + 20 per cent.), and the glycemic response over a period of six and one-half hours, was characterized by definite lowering of the acme point, very gradual decline, and the absence of any indication of a normal reaction pit or subsequent rebound. These results correspond essentially with those found recently in other cases of acute schizophrenic disorder, by Parsons and Raphael.[2] Negative responses were obtained with the Löwi, Csepai, and Ascoli[3] tests for adrenal function and also with the Ascoli and Brock-Kay[3] tests for hypophyseal function.

The blood platelet count was somewhat elevated when compared with the average normal (505,000 per cubic millimeter), and the bleeding time was decreased four minutes. Blood sugar tolerance (Janney-Isaacson schedule[4] and

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1. Bryant, J.: The Carnivorous and Herbivorous Types in Man, Boston M. & S. J. **172**:321 (March 4) 1915.

2. Raphael, T., and Parsons, J. P.: Metabolism Studies in Dementia Praecox and Manic Depressive Insanity, Arch. Neurol. & Psychiat. **8**:172 (Aug.) 1922.

3. Rabinowitch, I. M.: Metabolic Studies on a Case of Diabetes Insipidus, Arch. Int. Med. **28**:355 (Sept.) 1921.

4. Janney, N. W., and Isaacson, V. I.: A Blood Sugar Tolerance Test, J. A. M. A. **70**:1131 (April 20) 1918.

standard Folin technic) was definitely delayed and there was evidence of initial hypoglycemia, as had been noted also in other acute schizophrenic cases.[5] The figures were: 0.07 per cent. at the fasting level; 0.14 per cent. at the end of the first hour; 0.16 per cent. at the end of the second hour, and 0.11 per cent. at the end of the third hour.

The basal metabolic rate was consistently low, and ranged from —21 per cent. to —29 per cent., in spite of a tube-fed diet which contained 3,200 calories in twenty-four hours; definite anoxemia (Van Slyke) was noted both in the arterial (—15 per cent.) and in the venous (—30 per cent.) blood, although on the basis of the hemoglobin content this did not seem to be associated with deficiency in oxygen carrying power. Blood fragility[6] was found to be slightly, but consistently, increased, and the blood lipoid content (Hoag modification of the Bloor technic[7]) was somewhat diminished (0.5 per cent.). Hepatic function[8] was found to be definitely delayed; the phenoltetrachlorphthalein return time was thirty-four minutes as compared to the average normal interval of seventeen minutes.

Later Course and Examinations.—After about five months in the hospital, during which the patient had become profoundly emaciated, a gradual tendency toward improvement became evident. He began to eat and showed some affective response. From this time, a gradual increase in weight was noted until at the time of discharge, nine months after admission, the patient had gained 50 pounds. Mentally, improvement was almost as marked. The patient began to talk, played games, drew, painted, mingled with the other patients, and joined in the outdoor games. Yet this improvement seemed distinctly incomplete as he still occasionally showed mannerisms in gait, and was somewhat seclusive in reaction; there was continued evidence of intrapsychic conflict, manifested by persistent refusal to answer questions which concerned intimately personal problems, and by indications of a certain sullenness and dysaffect when such questions were asked. Nevertheless, it was very evident that vast improvement had actually taken place and, paralleling this, it was observed that the disturbances in the endocrino-autonomic and metabolic fields were also gradually disappearing. Particularly was this true of the vagotonia. A physiologic cross-section, completed a few weeks prior to discharge, indicated that practically normal responses were now obtained in all fields which had previously shown deviations.

The basal metabolism was now normal (+5 per cent.), as were the blood lipoid content (0.69 per cent.), hepatic function (19 minutes), arterial and venous blood-oxygen combining power, blood fragility, blood sugar tolerance except for an initial relative hypoglycemia (0.08, 0.12, 0.08, 0.07), blood platelet count (270,000 per cubic millimeter) and bleeding time (5.4 minutes).

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5. Raphael, T., and Parsons, J. P.: The Physiologic Level in Dementia Praecox, Am. J. Psychiat., to be published.

6. Greenthal, R. M., and O'Donnell, W. J.: Fragility of Red Blood Corpuscles in Infectious Diseases, Am. J. Dis. Child. **22**:212 (Aug.) 1921.

7. Hoag, L. O.: Personal Communication, University Hospital, Ann Arbor, Mich.

8. Aaron, A. H., Beck, E. C., and Schneider, H. C.: The Phenoltetrachlorphthalein Test for Liver Function, J. A. M. A. **77**:1631 (Nov. 19) 1921.

Responses to the Löwi, Csepai, Ascoli, and Brock-Kay tests were likewise normal. The reaction to autonomic pharmacodynamic reagents showed complete absence of vagotonia. In fact, there seemed to have developed a slight sympathetic preponderance, as the pilocarpin and physostigmin tests were frankly negative and atropin produced definite tachycardia (+ 50); epinephrin produced pronounced pallor, tremor, pulse acceleration (+ 65), blood pressure rise (+ 25) and glycosuria. At this time, too, it is interesting to note that the blood pressure had become definitely elevated as compared with the level on admission (systolic 120, diastolic 70). The body temperature was now quite normal (98 to 98.6 in the axilla), as was the vasomotor status except for a mild, persistent tendency to cyanosis of the extremities. There was no longer any evidence of hyperpigmentation.

DISCUSSION

In view of the familial setting and the apparently classical pathogenetic and clinical course, a diagnosis of acute catatonic stupor, of schizophrenic type, with subsequent remission, seems warranted. It is also permissible to assume the existence of a primary asthenic (carnivorous) habitus from the somatomorphologic deviations with associated vagotonic cardiovascular features which have been described.

The existence of a fundamental autonomic imbalance, which was at first definitely of the vagotonic type, and later, as recovery progressed, assumed that of a mild sympathicotonia, may be inferred during the first phase from: the bradycardia; hypopiesis; cyanosis; striking vasomotor disorder; hypothermia; coarse, thick pigmented skin; strongly positive pilocarpin and physostigmin reactions; lowered epinephrin and atropin sensitivity; and the generally depressed metabolic status. During the second phase imbalance may be inferred from: the mild tachycardia; slightly hyperpietic trend; improvement in the hypothermia, skin pigmentation and vasomotor disorder; and from the definite pilocarpin and physostigmin insensitivity, with markedly increased sensitivity to epinephrin and atropin. The significance of this reversal is admittedly more or less conjectural; but it obviously seems to be of the nature, either of a primary autonomic compensation, or a reflection of improved adrenal function. The actual development of such a clearly cut vagotonia upon a primarily asthenic basis may be construed as a corroboration of the assumption that a certain relationship exists between this habitus and clinical vagotonia.

That there seems also to have been a definitely endocrinic facet to the clinical structure, is obvious. During the preliminary or acute period, there was adrenal hypofunction accompanied, though to a somewhat less degree, by pituitary and thyroid inadequacy. During the recovery phase, there was gradual improvement in this state of hypofunction and, eventually, the development of a slight but definite hyperactivity

of the adrenal system. During the stupor, adrenal hypofunction was evidenced by the occurrence of the well marked vagotonic features[9] which have been described. As evidence of relative thyroid hypofunction, there may be noted: the general asthenic reaction and stupor; the coarse skin texture; bradycardia; low body temperature; low blood pressure; low blood sugar; diminished basal metabolism; relative insensibility to epinephrin; increased blood platelet count and shortened bleeding time. As evidence of diminished hypophyseal activity, there were the general asthenia; the cardiovascular disturbances; and the hypothermia, metabolic depression and negative response to the Ascoli and Brock-Kay tests. During the convalescent phase the change which had occurred is indicated by the practically normal pharmacodynamic and endocrinic responses; the wholly normal responses in the metabolic field; the marked general physical improvement; and the disappearance of the initial vagotonia with the gradual development of frankly sympathicotonic features.

The actual significance of this phasic alteration of endocrine function, especially in the autonomic field, is more or less speculative; but presumably it is associative rather than specifically primary or secondary in nature. At any rate, on this basis there appears to exist an intimate interrelationship between this endocrinic triad and the sympathetic and parasympathetic divisions of the autonomic nervous system. This is in accord with the observations of Brown,[10] Timme[9] and Cannon.[11]

As evidence of the general metabolic depression, essentially hypooxidative in type, which occurred during the acute stuporous period, there are: the consistently lowered basal response in spite of high caloric feeding; delayed sugar tolerance with initial hypoglycemia; relative hypolipemia; diminished blood-oxygen combining power; increased red cell fragility; and relative hepatic hypofunction; as well as the development of a generally asthenic state; depression of the cardiovascular field; and indications of lessened function of the adrenals, thyroid and pituitary. These findings, it may be of interest to note, appear to be in close agreement with determinations upon other schizophrenic subjects by Raphael and Parsons.[5] The question of the specific significance of the metabolic deviation is obviously also conjectural, particularly as to whether it is primary, or secondary to the endocrino-autonomic disorder.

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9. Timme, W.: Clinical Endocrinology, Neurol. Bull. **3**:3 (Jan.) 1921.

10. Brown, L.: The Sympathetic Nervous System in Disease, London, 1920, p. 23.

11. Cannon, W. B.: Evidence of Nervous Control of Some Internal Secretions, Arch. Neurol. & Psychiat. **6**:707 (Dec.) 1921.

SUMMARY

An analytic report is made of a case which presented definite indications of primary or fundamental asthenic habitus, the gradual development of an acute schizophrenic catatonia with stupor reaction, and almost complete recovery; and which further, in strikingly phasic association, on the physiologic level, presented marked vagotonia and hypoadrenalism, and, to a somewhat less degree, hypophyseal and thyroid inadequacy with evidence of general metabolic depression, essentially hypo-oxidative in type. These findings strongly emphasize trends that have been noted in other acute schizophrenic reactions.

PHENOBARBITAL (LUMINAL) TREATMENT OF INSANE EPILEPTICS

IRA A. DARLING, M.D.

WARREN, PA.

Phenobarbital (phenyl-ethyl-barbituric acid), under the name of luminal, was patented in the United States during 1912. It was accepted by the Council on Pharmacy and Chemistry of the American Medical Association and incorporated in New and Nonofficial Remedies during 1913. In this book it was reported as a useful hypnotic in nervous insomnia and conditions of excitement of the nervous system. No mention was made of its possible utility in the treatment of epilepsy.

As early as 1912, Hauptmann [1] reported tentatively favorable results from the use of this drug in treating a series of cases of idiopathic epilepsy. In 1913 Pécheux [2] had good result in ten cases of epilepsy. After this, numerous reports appeared in the foreign literature, all quite favorable in character. Fuchs,[3] Debrowski [4] and Kutzinski [5] were among those who wrote hopefully about the new drug. In 1919 Dercum [6] reported exceptional success in cases of mild idiopathic epilepsy. Grinker,[7] in 1920, reported favorable results in a series of one hundred cases treated by him since 1913. In this paper he calls attention to his reference to the use of this drug in discussing a paper read by Dercum before the Section on Nervous and Mental Diseases of the American Medical Association in 1916. During 1920 Cheinisse [8] reviewed the foreign literature and reported that the consensus of opinion appeared to be that this drug deserves the leading place in the treatment of idiopathic epilepsy. In 1921 Kirk [9] reported favorable results in a series of two hundred cases. Austin [10] reported forty-nine cases treated for a period of fifteen months, and was of the opinion that phenobarbital gave better results in the treatment of idiopathic epilepsy than any other drug so far used. Small [11] reported fifty cases, 80 per cent of which

1. Hauptmann, A.: Münch. med. Wchnschr. **59**:1907 (Aug. 27) 1912.
2. Pécheux, Alfred: Lille, 1913, No. 25, p. 100.
3. Fuchs, W.: München. med. Wchnschr. **61**:873 (April) 1914.
4. Debrowski, W. G.: Monatschr. f. Psychiat. u. Neurol. **36**:248, 1914.
5. Kutzinski, A.: Monatschr. f. Psychiat. u. Neurol. **36**:174, 1914.
6. Dercum, F. X.: Therap. Gaz. **35**:609, 1919; J. Nerv. & Ment. Dis. **50**: 168 (Aug.) 1919.
7. Grinker, Julius: J. A. M. A. **75**:588 (Aug. 28) 1920.
8. Cheinisse, L.: Presse méd. **28**:598 (Aug. 28) 1920.
9. Kirk, C. C.: Am. J. Insan. **77**:559 (April) 1921.
10. Austin, M. L.: Ohio State M. J. **17**:683 (Oct.) 1921.
11. Small, V. R.: Virginia M. Month. **48**:386 (Oct.) 1921.

improved under treatment. Hughes [12] reported thirty cases treated for one month, with reduction in number and severity of the seizures. Sands [13] treated sixty-eight insane, idiopathic epileptics with very satisfactory results. Foley [14] reported the result of treatment in fifteen men and twenty women who were under institutional care because of epilepsy. He stated that there was no reduction in the number of seizures during the three months in which the men were given phenobarbital instead of bromid; but that among the women there was a reduction from two hundred and five seizures in thirty days during the last month under bromid, to sixty-six seizures during the third month under phenobarbital. This prominent difference in the effect of the drug, drawn upon sex lines, must be carefully checked by other observations before being given serious credit. Foley further stated that "the severity of each convulsive attack of those having convulsions, was greatly increased. . . . we noticed a marked increase in the irritability of all cases under treatment and the irritability of some cases increased to a deep furor. The furors were more prolonged and intense than ever observed under the bromid treatment." Golla [15] treated one hundred and twenty-five patients with phenobarbital. Eighty-nine of these did better than when given bromid, four persisted in complaining of giddiness so that the drug had to be discontinued, two had urticarial rashes during early treatment that disappeared without the drug being discontinued. Fox [16] treated sixteen children and adolescents with combined phenobarbital and bromid, with varied effects on the intellectual condition of the patients. On the whole, his impression as to the value of the drug appeared quite favorable.

In 1912 and 1913 German physicians, using phenobarbital for its sedative effects, reported toxic action and rashes after even moderate doses. Blichert,[17] in July, 1913, reported signs of intoxication in five out of thirteen patients who were taking from six to nine grains (0.4 to 0.6 gm.) of phenobarbital twice daily. In addition to the intoxication, several of his patients developed transient rashes. Farnell [18] reported two patients with severe toxic symptoms after taking nine grains (0.6 gm.) and eighteen grains (1.2 gm.) respectively. These patients are described as "dreamy and sleepy . . . speech was slurring and scanning; . . . on attempting to walk she

12. Hughes, W. N.: Rhode Island M. J. **4**:157 (Dec.) 1921.
13. Sands, I. J.: Arch. Neurol. & Psychiat. **5**:305 (March) 1921.
14. Foley, E. A.: Illinois Instit. Quart., March 31 and June 30, 1921.
15. Golla, F.: Brit. M. J. **2**:320 (Aug. 27) 1921.
16. Fox, J. T.: Lancet **2**:558 (Sept. 10) 1921.
17. Blichert, E.: Ugesk. f. Læger **75**:1149 (July 3) 1913.
18. Farnell, F. J.: J. A. M. A. **61**:192 (July 19) 1913.

swayed." Both of these patients recovered within forty-eight hours. Haug [19] reported two patients, each taking a grain and a half (0.09 gm.) of phenobarbital three times a day, who developed toxic symptoms eleven days and four weeks, respectively, after starting to use the drug. These patients had high fever, diarrhea, mucous stools, (blood in the stools of one) and a scarlatiniform eruption over the entire body except the hands and face. Both patients recovered a few days after the suspension of the drug. Ruggles [20] reported toxic effect from a dose of three grains (0.2 gm.) daily. His patient showed slowing and slurring of speech, incoordination, tremor of the lips, and lack of facial expression. Recovery took place within a few weeks. Rosenberger [21] reported a death following the use of phenobarbital and opium combined. There have been many other reports on the treatment of epilepsy with phenobarbital and the toxic action of the drug, but those quoted are typical of the whole and are sufficient to indicate the trend of opinion as to its efficacy and the dangers of indiscriminate, ill advised use of the drug.

It is the purpose of the present report to show the results of treatment with phenobarbital in a series of male patients at the Warren State Hospital for the Insane. The patients are all classed as insane epileptics and require hospital care because of pronounced dementia or periods of extreme and dangerous violence. None of the series can be considered of the mild or incipient type, and nearly all have been subject to seizures for many years. All of the patients treated are considered as belonging to one of four groups: idiopathic, traumatic, senile, or syphilitic. For the purpose of this report epilepsy will be considered as meaning any illness in which the most prominent symptom is clonic convulsive states associated with unconsciousness. When epilepsy is modified by the word "idiopathic" it will be understood that careful physical, neurologic, mental, and laboratory examinations have failed to reveal any probable cause for the convulsive attacks. Traumatic epilepsy is diagnosed only when definite evidence of cranial injury can be demonstrated and associated with the development of the seizures. Senile epilepsy is diagnosed when the seizures develop well after middle life, and when there are other clear signs of cerebral sclerosis. Epilepsy is considered syphilitic when there is, or has been, laboratory evidence of syphilis during examination of the spinal fluid.

During January, 1920, following the earnest solicitation of Dr. Dercum, phenobarbital was tried in the treatment of fifteen hospitalized, insane epileptics of the idiopathic type. The initial results were

19. Haug, W.: München. med. Wchnschr. **66**:1494 (Dec. 26) 1919.
20. Ruggles, A. H.: Arch. Neurol. & Psychiat. **6**:234 (Aug.) 1921.
21. Rosenberger, F.: Med. Klin. **15**:1150, 1919.

favorable enough to interest me in continuing the treatment and adding others to the phenobarbital group. In the discussion of a paper by Kirk,[9] read before the 1920 meeting of the American Psychiatric Association, Dr. H. W. Mitchell presented the results obtained in this preliminary group of cases. He said, "The most noticeable effect upon the patients under observation was the improvement in their daily reactions to ward life. There was much less irritability and consequent quarreling, a great reduction in the minor injuries sustained during seizures, and no exhibition of the periods of clouded consciousness which the same patients had manifested frequently before the use of the drug. So far as could be detected, there were no noticeable bad effects from the use of the drug." The effect upon the number of

Chart 1.—Number of seizures in fifteen men during eight months under treatment with: *C*, no drugs; *P*, phenobarbital; *P B*, phenobarbital combined with bromids.

seizures is indicated in Chart 1. The dots represent the average number of seizures for the entire group of fifteen patients during each of the eight months covered by the study. As will be seen, the first four months were used as a control period during which no drug treatment was employed. In the fifth month a combination of phenobarbital and bromid was given, and a remarkable reduction in the average number of seizures followed. During the sixth month phenobarbital alone was used, and there was a moderate increase in the number of attacks. During the seventh month all drugs were omitted and the number of seizures increased a little more. During the eighth month when phenobarbital alone was used, there was a reduction in the number of seizures.

Following this initial trial of phenobarbital, a standardized technic of administration was developed. Every morning, before breakfast, a saline laxative is given. The type of laxative has been changed from time to time and the dosage varied according to the requirements of the individual patient. Midway between the noon and evening meals one and one-half grains (0.09 gm.) of phenobarbital are administered, preferably in capsule. The phenobarbital is given only five days in each week. For convenience and clearness, the nurses' instructions read that it is to be given every day except Saturday and Sunday of each week. The diet is regulated along the lines recommended by Spratling.[22] Regularity of time, moderation in quantity, full mastication, and limitation in amount of the richly nitrogenous foods are considered the most important requirements. Some patients require a larger amount of phenobarbital to obtain the best results and such increases are made when indicated. Divided doses have been tried; but a single dose, given in the afternoon when the stomach is empty, is thought to be the best mode of administration. As much as four and one-half grains (0.25 gm.), five days in each week, have been given for several weeks without ill effects; but three grains (0.2 gm.), given five days in each week, have caused mental dullness and a slight rash. No toxic effect has been observed from the use of a grain and a half (0.09 gm.) administered in this manner. Whenever the larger doses are used it is essential that the nurse or the family be carefully instructed concerning the toxic symptoms, and that the physician be informed immediately if any of them are even suspected. Further, it is necessary for the physician to keep constantly in mind that he is prescribing a powerful drug, and to insist upon frequent, personal observation of his patient, especially if more than a minimum dose is used.

Beginning Feb. 1, 1921, phenobarbital was given to thirteen men with idiopathic epilepsy. Nov. 1, 1922, twelve of these patients were still in the hospital and receiving the same type of treatment. The regimen during the entire period was the same each month except during February, April, and July of 1922. During February twenty grains (1.25 gm.) of mixed bromids daily were substituted for the phenobarbital with the purpose of observing the effect of change in treatment. In April the same change was made because there was difficulty in obtaining phenobarbital. In July phenobarbital was given to some patients and mixed bromids to others. One patient died during April in status epilepticus. This man averaged seventeen seizures per month for years prior to taking phenobarbital and had developed status

22. Spratling, W. P.: Epilepsy and Its Treatment, 1904, W. B. Saunders Company, p. 354.

epilepticus several times. In January, 1921, while taking phenobarbital, a similar condition developed; and in April, 1922, while taking mixed bromids, the final attack occurred. The ten months which elapsed between March, 1921, and February, 1922, during which he was taking phenobarbital, were the most comfortable he had had for years.

An attempt has been made to show in graphic form the average number of seizures of this group during each of the months covered by this report, and to compare these numbers with the monthly average for the group when no specific drug treatment was used. In making this graph a careful estimate of the average number of attacks per month for each patient prior to taking phenobarbital was made by consulting hospital records, or by interviews with members of the man's family. A period of at least three months was considered in each instance. The average number of seizures per month for each of the thirteen men were added together and the result was divided by thirteen. This gave eight seizures per month as the average, or norm, for this particular group; and it is indicated by the straight line in the graph. The number of seizures of each patient, during each month was then added, divided by thirteen, and this result compared with the norm for the group. Nine of this group had a lower average number of seizures per month while being given phenobarbital, three showed no definite change, and one had more seizures than before.

The second group is very similar to the first, the main difference being that the patients have been treated only from eight to thirteen months. It is made up of twelve men, seven, who have been in the hospital for a number of years, and five who have been recently admitted. Before treatment was started this group averaged nine seizures per month. Chart 3 compares this norm with the group averages for each of the months covered by this report. Changes from the routine treatment were made during the months of February, April, and July, as described in the explanation of Chart 2. Eleven of these men had a marked reduction in the number of seizures while taking treatment and one continued to have about his usual number of attacks. As will be seen by consulting the graph, there was a quite distinct rise in the average number of seizures during the months that bromid was substituted for phenobarbital. Six of these patients had a distinctly smaller number of seizures when taking phenobarbital than when taking bromid. The other six appear to have done equally well with either form of treatment.

The next group is made up of men who have developed grand mal epileptic attacks following cerebral trauma. None of the injuries is recent, and all of the patients have had the benefit of operation, or at

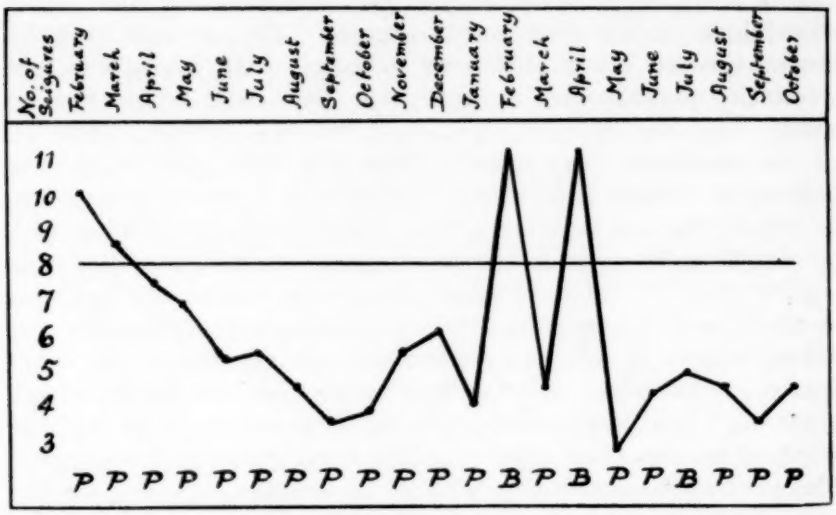

Chart 2.—Average number of seizures in thirteen men under treatment with: *P*, phenobarbital; *B*, mixed bromids. The horizontal line represents the previous average. The same symbols are used in Charts 3, 4, 5 and 6.

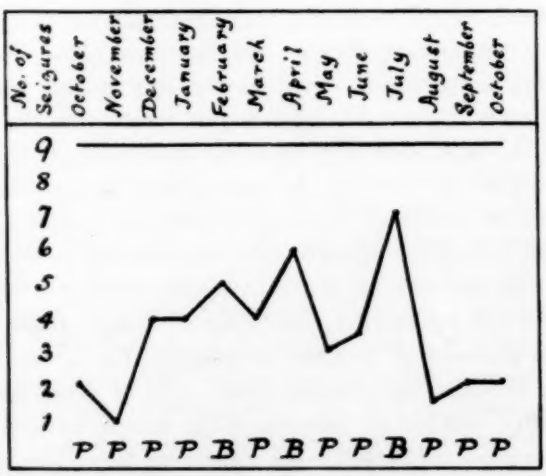

Chart 3.—Average number of seizures in twelve men.

least of competent surgical advice. Several have submitted to three or four operations. The average number of seizures for this group before taking treatment was found to be eleven per month. Treatment with phenobarbital was started Oct. 1, 1921, and has been continued since that time, except for three months—February, April, and July of 1922. During these months the treatment was the same as described in the explanation of Chart 2. The chart shows that there has been a great reduction in the monthly average of attacks. During the months that bromid was substituted there was some rise in the number of seizures, but no pronounced increase. Two of the patients had many

Chart 4.—Treatment of six men with grand mal seizures after cerebral traumatism.

more attacks during the months that bromid was used, the other four did about equally well with either type of treatment.

The fourth group is made up of six cases diagnosed senile epilepsy, that have been treated for from eight to thirteen months. The results of treatment in the individual cases of this type were not so good as the graph indicates. One of the old men averaged ten seizures a month without treatment; but, while taking phenobarbital or bromid, has had only four seizures a month. The other five had from one to five seizures a month prior to treatment, and they have all continued to have about the same number since. Chart 5 compares the monthly averages of this group with the group norm in the same manner as the preceding charts.

Two patients have been treated who have typical grand mal attacks associated with the usual type of epileptic mental deterioration, but who have had, at some time during their period of hospital care, positive blood Wassermann reactions and syphilitic colloidal gold curves. Neither of these men has had positive Wassermann reactions with the spinal fluid, nor do they have the neurologic signs ordinarily present in general paralysis or cerebrospinal syphilis. Antisyphilitic

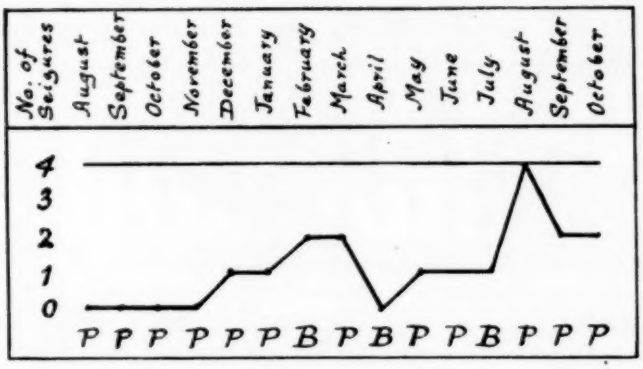

Chart 5.—Treatment of six cases of senile epilepsy.

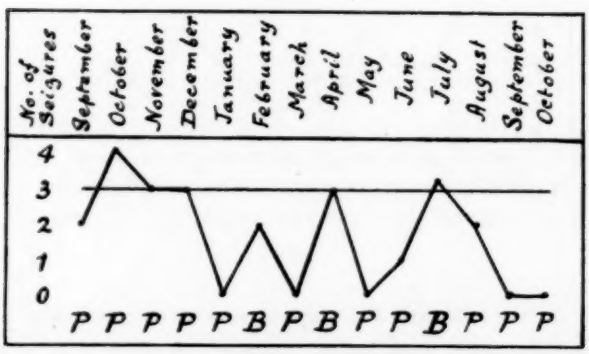

Chart 6.—Treatment of two epileptics who have given positive Wassermann tests at some time.

treatment has been tried with little, if any, effect upon the number of seizures, though there has been improvement in the laboratory findings. Chart 6 compares the average number of attacks per month of this group with the group norm, in the same manner as the preceding charts. There appears to be some reduction in the number of seizures, but the frequency of the attacks is so irregular and the group so small that little information can be obtained from the data at hand.

SUMMARY

1. Phenobarbital has a cumulative effect that appears to be successfully combatted by a break of two days in each week during its administration.

2. A sudden break in the administration of phenobarbital is sometimes followed by a series of seizures. There is much less danger of such trouble if bromid is given as soon as the phenobarbital is withdrawn.

3. One and one-half grains (0.09 gm.) given five days in each week appears to be a safe dosage. If larger amounts are given, very careful observation is necessary to detect possible toxic symptoms early and to prevent the more serious disorders.

4. The use of this drug may be followed by: rash, simulating measles or scarlet fever; symptoms like those of alcoholic intoxication; severe, cholera-like diarrheas; mental hebetude; delirious states; and other like troubles.

5. Favorable results were obtained from the administration of phenobarbital in cases diagnosed as idiopathic and traumatic epilepsy. The results in cases diagnosed as senile and syphilitic epilepsy were doubtful.

6. Phenobarbital is not to be considered as a "cure" or specific for epilepsy.

7. Phenobarbital and bromid may be combined and better results thus obtained in selected cases.

8. Each case should be considered as an individual problem and phenobarbital, bromid, or a combination of the two used according to the results.

THE PATHOGENESIS OF EPILEPSY

A CRITICAL REVIEW WITH A NEW INTERPRETATION OF THE AVAILABLE DATA *

MICHAEL OSNATO, M.D.
Associate Professor of Neurology, New York Post Graduate Hospital and Medical School; Associate in Neurology, Columbia University
NEW YORK

The conceptions of the causes of epilepsy are many and confusing. Any discovery which reveals the causes underlying the convulsive manifestations will tend to clarify the situation. I have little sympathy with the view so often expressed of late that the mental (dementia), and even the paralytic and other somatic disorders of epilepsy, are secondary to the psychogenically determined convulsive attacks. The more I study the experimental work and the anatomic, biochemical and pathologic data bearing on the question, the more tenaciously do I hold to the belief that if the convulsions in epilepsy are once satisfactorily explained, the whole problem will be placed on a sound basis.

While it is not possible to synthesize all theories of the causation of epilepsy, the psychogenic factor may be readily assimilated in our discussion. The staunchest upholder of the psychanalytic conception is Dr. L. Pierce Clark.[1] He believes that epilepsy is the result of a peculiar personality defect which is constitutional. This defective make-up is characterized by great egocentricity, emotional poverty and hypersensitiveness. Thus, the epileptic is handicapped in his ability to make even fundamental life adaptations and adjustments. To the stresses which constantly accumulate, he reacts by convulsive seizures. This allows him to escape from reality and responsibility and aids him to protect his personality from the demand to cope with his environment. According to Clark, therefore, treatment cannot be successful until the approach is made by psychobiologic, analytical means. In evaluating the psychogenic, emotional factor, I venture to quote remarks I made when Dr. Clark's last paper on this subject was read at the June, 1922, meeting of the New York Neurological Society.[2]

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* Read at meetings of the Clinical Society of the Post-Graduate Hospital, Oct. 6, 1922, and of the New York Neurological Society, Nov. 14, 1922.

1. Clark, L. P.: A Psychological Interpretation of Essential Epilepsy, Brain **43**:38 (May) 1920; Treatment of the Epileptic, Based on a Study of the Fundamental Makeup, J. A. M. A. **70**:357 (Feb. 9) 1918; Clinical Studies in Epilepsy, Psychiat. Bull., January, 1916, April, 1916, and January, 1917; Some Suggestions for More Accurate Mental Therapy in Epilepsy, J. A. M. A. **71**:255 (July 27) 1918.

2. Clark, L. P.: Arch. Neurol & Psychiat. **8**:319 (Sept.) 1922.

"I believe that Dr. Clark stated that the delirium in petit mal was of the functional type because its content dealt with the everyday life experience of the individual. I do not think that is any criterion. All delirial productions deal with ordinary life experiences, with what is in the consciousness. Therefore, this does not prove that the delirium in petit mal is functional and not organic. I think there is danger in laying too much stress on the makeup and personality as determining the mental disease from which the patient suffers. The three points which Dr. Clark emphasizes—egocentricity, emotional poverty and hypersensitiveness—are not different from those found in the personality of patients with dementia praecox. The type of reaction is influenced by the makeup, but this does not cause the disease itself. Dr. Clark said that a tyro can pick out the epilepsy makeup, but that the epileptic patient may have minor degrees of the same attributes and that only the carefully trained physician can bring these out. The same qualities that are supposed to belong to the epileptic makeup are found in the characters of many people. Why should the mechanism be different in epilepsy if it is of psychogenic origin? Why should the psychologic mechanism work differently in epilepsy and express itself in convulsive manifestations which are objectively and by various chemical and other means so readily differentiated from the convulsive manifestations of hysteria?"

The psychogenic theory of the causation of epilepsy does not explain why other nonepileptic individuals who are egocentric, emotionally defective and hypersensitive do not have the convulsive episodes of the epileptic. Neither does it explain the epilepsies of cerebral arteriosclerosis, trauma, the Jacksonian attacks, or the convulsions occurring in general paralysis, cardiorenal disease, endocrine disturbances (possibly pituitary, status thymico-lymphaticus), and the focal epilepsies of brain tumor, brain abscess or the epilepsies in animals (monkey).[3] In all fairness, however, these psychologic explanations of the epileptic constitution, cannot be entirely disregarded. It requires only the barest reference to the work of Crile [4] and Cannon,[5] to deter one from adopting such an attitude. These authors have shown that painful and prolonged emotional states cause increase of the adrenal secretion in the blood, and, with the addition of fatigue, result in toxic changes which are destructive to liver and brain cells. The blood in these conditions also manifests increased coagulability and sugar content. In view of the work on the toxicity of the blood in epilepsy, to be discussed later, one cannot too hastily disregard this situation in its possible relation to the convulsive manifestations. The liver is now known to produce a pressor and cardio-accelerator protein [5] in response

3. Sherrington, C. S.: Stimulation of the Motor Cortex in a Monkey Subject to Epileptiform Seizures, Brain **41**:48 (May) 1919.

4. Crile, G. W.: Boston M. & S. J. **153**:893, 1910; also many other more recent publications in The Journal A. M. A., 1910-1921.

5. Cannon, W. B.: Bodily Changes in Pain, Hunger, Fear and Rage, New York, D. Appleton & Co., 1920, p. 187. New Evidence for Sympathetic Control of Some Internal Secretions, Am. J. Psychiat. **2**:15 (July) 1922.

to sympathetic stimulation (hepatic nerves). Insufficient and inefficient personalities would yield more promptly to the disturbing emotional factors which produce these phenomena than more stable individuals.

The mechanical and vascular theories of the pathogenesis of the convulsions in epilepsy are satisfactorily summarized by Percy Sargent.[6] Most of our knowledge concerning this phase of the subject is derived from work on laboratory animals by Russell,[7] Sherrington and others, and on human beings by various surgeons including Sargent, Krause and Cushing.

The most reliable data point toward the vascular system, either alone or as a carrier of toxic products, as the offending element in epilepsy. Some believe with Sargent [6] that the vascular disorders are due to disturbance of the sympathetic-autonomic control of the cerebral cortical vessels, while others incriminate the endocrine or other biochemical intoxicants carried to the cortex in the blood stream, as the primary factor in the causation of the convulsive seizure. These toxic substances may be manufactured locally in the brain by the break-down of cortical tissue in disease (arteriosclerosis, general paralysis, uremia, the convulsions of alcoholism and of status thymico-lymphaticus, etc.).

Sargent noted "the striking rapidity with which visible circulatory changes may occur in response to various disturbing causes." It was not the congestion or anemia of the brain as a whole, but the local variations and abnormalities observed in cases of trauma and brain tumor with epileptic manifestations, which made him certain that "if there is a fundamental precipitating cause for all convulsive attacks, any hypothesis which does not take into account the pathogenesis of fits originating in the neighborhood of a gross lesion, must fail to touch that essential point." [6]

Sargent agrees with Russell, who first drew an analogy between the experimental animal in a condition of decerebrate rigidity and the tonic spasms of the epileptic in the initial tonic, rigid phase of the convulsive seizure; and, for the moment, the unconscious rigid epileptic is comparable to the animal whose cerebral circulation has been shut off. Of course, this does not account for the clonic movements which may follow. In laboratory animals, as many have observed, when the cerebral circulation is cut off, clonic convulsive movements supervene.[8,9]

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6. Sargent, Percy: Some Observations on Epilepsy, Brain **44**:312 (Nov.) 1921.

7. Russell, A. E.: Goulstonian Lectures, London, 1909.

8. Starling: Human Physiology, Philadelphia, Lea & Febiger, pp. 984, 989, 990, 1002, 1003 and 1085.

9. Stewart, G. N.; Guthrie, C. C.; Burns, R. L., and Pike, F. H.: The Resuscitation of the Central Nervous System of Mammals, J. Exper. Med. **8**:289, 1906.

Pike,[9] ten years ago, shut off the cerebral circulation of cats by tieing off the internal carotid and vertebral arteries close to the subclavian. Immediate unconsciousness and paralysis of respiration (asphyxia) occurred; to prevent death of the animal, artificial respiration was kept up for the eight or ten minutes during which the occlusion was allowed to continue. At the end of this time, the arterial sutures were loosened and the circulation was resumed. Immediately the animals were thrown into a series of convulsions, which lasted for days. Any jarring, stroking of the fur, or even loud noises, were sufficient to cause typical convulsions, a tendency which at times lasted for weeks.

Without developing the idea further at this point, it must be remembered that cells cut off from their blood supply even momentarily show a change in reaction toward acidity. During asphyxia and violent exercise, lactic acid is formed in the muscles and appears in the blood and urine. Cuneo has shown that, in acid mediums, the normal nucleohistone content of brain and other cells, (leukocytes) is capable of breaking down into nucleinic acid and proteoses (albumoses). These latter substances are capable of causing convulsions, whether they are painted on the cortex or are injected intravenously. In connection with the experiment of Pike, it has been noted in a few cases of human epilepsy that the tonic phase of the fit occurred coincidentally with arrest of the circulation, while the clonic phase was ushered in with the resumption of the radial pulse and the heart beat.[6]

The clonic movements which follow the tonic spasm, have the same origin as the motor mechanism which causes the Jacksonian fit. These Jacksonian movements are exactly like those produced by experimental faradization of the motor cortex and are not preceded either by the tonic phase or by loss of consciousness. This is the chief objection to the theory that the epileptic convulsive attack is caused in its entirety by the vascular disturbances described by Sargent in his cases of traumatic epilepsy. Sargent and others have repeatedly called attention to the fact that unconsciousness is the first sign of occlusion of the cerebral circulation. The theory is advanced that the clonic movements are caused by the gradual and, at first, insufficient resumption of the blood supply in the constricted cortical vessels, due to defective autonomic control of the vasomotor mechanism. An objection to this is that it has not been proved that there is any active vasomotor control of cerebral vessels.

Cushing noted that epinephrin painted on the pial vessels blanches them, locally, just as does faradization. Sargent [6] and Sherrington, together, observed that, when a faradic stimulus of strength sufficient to cause an epileptiform seizure was applied to the brain cortex of human beings and animals, the pia mater could be seen to blanch. One

can hardly call this satisfactory proof of vasomotor control of cerebral blood vessels. Epinephrin [8] has the power to constrict vessels stripped entirely of nervous connection. In faradization, there are undoubted chemical changes which take place in the propagation of electrical stimuli, the results of which may act locally on the vessel walls just as does epinephrin, independently of any action of the alleged sympathetic-autonomic control. At any rate, Sargent makes the important deduction that vasoconstriction is the basic principle underlying the convulsions in the cases of traumatic epilepsy on which he operated.

All of these patients manifested epileptiform attacks soon after severe craniocerebral injuries. These injuries resulted in strong and rather extensive adhesions between the scalp, the meninges and the brain. The pathologic variations in the vasomotor control of the cerebral vessels in these cases cause rapid changes of vascular supply, which are sufficient in themselves, he thinks, to explain the recurrences of the convulsive phase of epilepsy. The severe manias, the deliria, the confusions, the attacks of petit mal of the Jacksonian type, all of which may occur without the characteristic loss of consciousness, etc. of the typical epileptic attack, cannot be explained in this way. Neither is the mental deterioration of advanced epilepsy satisfactorily explained. Therefore it is hazardous and even unnecessary to say that "it may be that the search (for the cause of idiopathic epilepsy) transferred from the barren field of neurohistopathologic investigations of the cortex to that of the autonomic nervous system, will prove more fruitful." Such a statement should have awaited absolute proof that the autonomic nervous system controls the cerebral circulation. This is especially true in view of the certain knowledge which we possess [8] that the products of metabolism have a very definite action on peripheral blood vessels. Neither should one too hastily discard as of no value the work of Alzheimer [10] and others on the neurohistopathology of the cerebral cortex in epilepsy.

It is important to review briefly the results of stimulation of the cortex of human and animal epileptics. The most important observations are those of Fedor Krause (1911), Sherrington,[3] Sargent,[6] and Gordon Holmes, on individuals suffering from Jacksonian fits, without gross visible lesions discoverable at operation. It was found that faradization of the epileptogenous zone alone elicited the fits, while stimulation of the rest of the cortex produced only the appropriate movements, even though the nature and duration of the current was the same. In Sherrington's monkey [3] the epileptogenous areas were the tongue area of both sides, but the attacks were much more easily provoked from

10. Alzheimer: Ein Beitrag zur pathologischen Anatomie der Epilepsie, Monatschr. f. Psychiat. u. Neurol. **4**:367, 1898.

the right side. A minimal faradic stimulus applied over the tongue area of the right cortex produced epileptoid seizures beginning in the tongue, which continued after the stimulus was withdrawn. These seizures, in response to faradization, never extended beyond the face and tongue. The animal's spontaneous attacks, however, were left-sided and, occasionally, generalized. It was impossible, in either the human or monkey epileptic, to provoke a Jacksonian attack of any magnitude. The limbs never took part in the seizures. This is explained on the theory that the depth of the narcosis used prevented the spread of the convulsions. This explanation however is not adequate, since something was lacking under the experimental conditions which was present when the subjects had their attacks spontaneously. This hitherto unknown influence accounts for the difference in the type of convulsive seizure. The probable nature of this factor will be discussed later.

In the experimental work of Sherrington, Krause, Horsley, Leyton, and others, one finds great agreement in the conclusions. First, there is a wide variation among animals in the ease with which the spread of the Jacksonian-like seizure is produced by faradization. Second, the excitability of the cortex is increased by repeated stimulation, so that a weaker current will evoke a spread. Third, the area from which a given movement may be obtained can be extended considerably by repeated stimulation. These facts were confirmed in the human being by Gordon Holmes and Sargent,[6] who faradized the cortex in front and behind the Rolandic fissure in the case of a man suffering from Jacksonian epilepsy which was caused by craniocerebral injury. As a result of this experiment, these observers concluded that the movements caused by electric stimulation of the cortex are like the movements of the epileptic attack, in that they are possessed of the quality of purposive coordination (the fractional movements of Sherrington), but are not completely purposeful. A Jacksonian fit is a series of these fractional movements, devoid of mutual purpose, and "determined in point of sequence only by the relative anatomic position of cortical areas in which they are represented . . . so that the tongue may be bitten, due to the unnatural sequence of tongue protrusion and jaw closure." [6] In this regard, the movements caused by electrical stimulation are exactly similar to those of the epileptic convulsive seizure. No purposeful movement, however simple, can be brought about by faradization of the cortex. This discussion eliminates the interpretation of the psychanalysts that the epileptic fit is a subconscious, symbolically purposeful act.

Sargent believes that the early fits which follow head injury are due to acute vascular disturbances: small hemorrhages, edema, injury to cortical tissue with inflammatory reactions, the effects of recurring sepsis, etc. The adhesion of the scars, binding the scalp to the brain

tissue, is the vital factor in those cases in which the attacks occur a long time after the injury. The initial disturbances of the vascular supply are caused by traumatic thrombosis and strangulation of vessels in the course of the severe scar formation in the cortex, and between the cortex and the scalp, or by adhesions between previously infected membranes and the cortex. These infections occur at the time of the infliction of the wound. After the acute phase, during which attacks are apt to recur frequently, there is a prolongation of the intervals and the explanation for the attacks must be sought in the vasoconstriction which is locally produced when the brain is pulled upon and distorted by the adherent scalp.

Normally every time the head moves the brain moves within the skull. This has been proved by frozen sections and by a kinesiometer. This movement is made possible by the space which exists between the dura and the arachnoid. When the brain is anchored to the scalp by adhesions, this movement is restricted, and there occurs at the point of anchorage a pull upon the brain which "mechanically or possibly by causing reflex vasoconstriction" produces a "momentary local anemia in the damaged brain and so initiates a fit." [6]

This reasoning, while it appeals rather strongly at first, leads to certain questions. Sargent reviewed over eighteen thousand cases of craniocerebral wounds with skull defect, which resulted from injuries sustained in the late war. Of these approximately only eight hundred (4.5 per cent.) developed epilepsy. Why? The answer is that "a given stimulus is not effective for all brains and it is necessary to assume in those patients who develop fits, a tendency to epilepsy," from what is vaguely called, "a relatively low degree of stability of the nervous tissue." [6] A case is cited as an example of what Sargent means by his vague characterization. This case is also important from the standpoint of the effect of prolonged emotional situations and fatigue (psychogenic factor) in the production of epileptic seizures.

The patient was a man of 35, who had been wounded in the forehead at the age of 15. He was operated on for depressed fracture immediately, with a resultant large craniocerebral defect. He remained well for twenty years until he joined the British Motor Transport Service in France in 1915. After six months, he had his first general convulsion, and then two dozen between that time and the date of his admission to the hospital. The brain bulged through an irregular opening in the right frontal bone. At operation, in May, 1920, the scalp was dissected away from the dura and the latter was separated an inch or more from the bone around the edge of the opening. As in most of the cases of this sort operated on by Sargent, he placed a thin sheet of celluloid over the dura, between it and the inner surface of the skull. A thicker sheet of celluloid was used to close the opening. Ten weeks after the operation, the patient had one attack and has had none since—(Sargent's paper was read Oct. 13, 1921).

The operator's interpretation of this case is that "although for twenty years this patient had a cranial defect through which the brain was anchored to the skull, the local lesion had been insufficient to cause a fit until nervous stability had been lowered by the stress of warfare." It seems, however, that a more complete explanation would have to consider conceptions of Clark concerning the psychogenic origin of epilepsy, and those of Cannon and Crile based on their work on the conditions of painful emotions, fear, anger and fatigue. It may be that not only epinephrin but also other toxic substances are produced in the severe affective states mentioned and in fatigue, which give rise to the convulsive phenomena of epilepsy.

The proteoses which Cuneo [11] names as the convulsion-producing substances in epilepsy, are capable of causing epileptiform attacks when painted over the motor cortex. Cushing has shown that epinephrin may cause the same phenomenon. Lactic acid, a prominent abnormal constituent of the blood of individuals after excessive muscular exercise or under conditions of deficient oxygen supply,[8] causes convulsions when injected intravenously.[11] Whatever the toxic agent may be, there certainly is some more tangible factor than that of the "stability" of the nervous system, which determines the presence of epilepsy in individuals who have suffered craniocerebral wounds. If this were not so, it would be hard to explain why only 4.5 per cent. of a large number of these cases have developed epilepsy.

Reed [12] undoubtedly had, in the light of Cuneo's work, a useful and helpful thought regarding the pathogenesis of the epileptic seizure. He was partly correct when he placed the causes for the origin of the epileptic attacks in the intestinal tract. According to Cuneo, however, the trouble is to be found in disordered carbohydrate metabolism in the small intestine and in the liver. Reed, incriminated the large gut, and with his co-workers insisted that all the pathology of epilepsy was contained therein. They therefore resected the large intestine in epileptics with much confidence and assurance. Much has been said concerning pathologic changes in epileptic brains, and neurohistopathologists have recently made important contributions to this subject. It seems certain, however, that the primary pathologic change is chiefly biochemical and metabolic, the changes in the brain structure being secondary. There is no lack of analogous situations in other central

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11. Cuneo, Gerolamo: Biochemical and Biological Researches on the Pathogenesis of Epilepsy, Riv. sper. di freniat. **45**:408 (Jan. 31) 1922; Biochemical and Biological Researches on the Pathogenesis of Epilepsy, ibid. **40**:837 (Nov.) 1914.

12. Reed, A. L.: Diagnostic Methods and Pathologic Constants in Idiopathic Epilepsy, J. A. M. A. **66**:336 (Jan. 29) 1916; Constipation and Intestinal Infection in Epileptics, ibid. **67**:1157 (Oct. 14) 1916.

nervous system disorders. In at least one very well understood condition, Wilson's disease, there appears to be an intimate connection between the pathologic changes in the liver and those in the brain. There, too, a toxic substance of unknown nature seems to have originated in the liver, or at least to have left its most damaging effects there and in the basal ganglions, and to have produced less severe damage in other parts of the brain, including the cortex.

Cuneo began his work in the laboratory for experimental pharmacology in the University of Genoa, in 1915. Since that time, he has devoted himself continuously to this problem and only recently has begun to seek cooperation in applying his conceptions practically in a therapeutic way. He first demonstrated the presence of a toxic substance in the blood of epileptics who had recently had a convulsion. He identified this substance with the proteoses. It was not found in the blood of normal individuals nor of those ill with other conditions, and never in epileptics in the intervals between attacks. He showed that the urine of epileptics who have recently had a convulsion, contains a total organic acidity of 80 per cent instead of the normal 5 per cent. In some cases these ammoniacal nitrogenous salts were found to constitute even 100 per cent. of the total acidity in the urine. He demonstrated in epileptics a retention of total nitrogen, an increase in the nitrogen content, and continuous acidity of the feces.

In order to explain these phenomena, he investigated the chemistry of protein metabolism. In the normal individual, organic acids are oxidized and are capable of reduction to carbon dioxide and water. Neither they nor the proteoses are ever found in the normal blood. The problem became more important to solve when he found that the proteoses introduced into the blood of experimental animals produced convulsions, strictly comparable to those of epilepsy.

Proteoses exist only in the gastro-intestinal tract as a result of the process of digestion of proteins. What happens when they are changed during further protein metabolism, is not clear. Cuneo, at first, was tempted to assume that because of altered absorptive properties in the intestines, the proteoses entered the circulation unchanged. In testing out this theory of the proteosemia (albumosemia) of epilepsy, Cuneo administered a protein rich diet (meat almost exclusively), to one large group of epileptics, and, to another, a preponderatingly carbohydrate diet. If it was true that in epileptics, there existed a defect which made it possible for the intestine to absorb proteoses in an unaltered state, Cuneo argued that those patients on a meat diet should become decidedly worse, while those placed on the carbohydrate diet would be expected to improve. Exactly the opposite took place. The epileptics on a protein diet improved, the acidosis practically disappeared, the attacks became less severe and occurred at longer intervals; while

those on a carbohydrate diet had an increase (percental) in the acidosis, and the number and severity of convulsions were greater. It was plain, therefore, that the protein metabolism was not responsible. This view was further supported by the observation that peptones, another product of protein metabolism, were never found with the proteoses in the blood of epileptics. The next step was to clear up the question of the connection between the formation of proteoses and the intense acidosis, and the possible relation of both to the ingestion of carbohydrates. The author experimented with monosaccharids (glucose), disaccharids (cane sugar, lactose, maltose) and polysaccharids (starches). He found that while glucose, cane sugar and lactose, given with milk, do not produce acidosis, the starches administered as rice, paste, bread, chestnuts, potatoes, etc. produced an obvious increase in the elimination of organic acids in mild cases and an overpowering increase in severe cases. This, Cuneo explained by the fact that glucose is absorbed as such, without transformation; the disaccharids divide promptly by fixation of one molecule of water, into two molecules of sugar and are thus absorbed as glucose. The polysaccharids, however, being amorphous and having a higher molecular content, must be reduced, by the action of amylolytic ferments, to the simpler disaccharid, maltose, which, in turn, is divided by the action of maltase through hydration into two molecules of glucose before absorption can occur. The cause of the acidosis of epilepsy, therefore, must be sought in this first phase of the metabolism of starchy substances, that is, in the stage when the starch is transformed into maltose. The second stage, namely, the transformation of maltose into glucose, goes on in a perfectly normal way. It is in this first stage that the organic acids are formed.

Cuneo points out that the formation of organic acids in this stage of the fermentation of starches, frequently occurs not only in the process of digestion, but also, for instance, in the industry of brewing beer. Great care is taken to prevent the formation of these acids, because their presence causes turbidity, and a diminution of the alcohol content. The offending organic acids are acetic, butyric, lactic, tartaric, etc. Their production is favored by an insufficient amount of amylolytic ferment and may occur even in normal individuals, but the final disposition of these acids is different in the epileptic. In normal individuals, the acids are rendered innocuous, because they are changed into salts by the alkaline substances found along the paths of absorption. They are then oxidized into ammonium carbonate, which, when dehydrated, becomes urea if the salts are ammoniacal; or if they are sodium salts, the organic acids are changed into sodium carbonate. This is the substance which serves to maintain the alakalinity of the intestines.

These acids or acid organic salts which are transformable into carbon dioxide and water, are not normally eliminated as such, but are oxidized into urea and sodium carbonate. In the epileptic, however, this does not occur, for the organic salts are found unoxidized in the urine. Thus, this very important source of alkalization, does not develop or is deficient. As confirmation of this point, Cuneo points to experiments in which he administered equal doses of sodium acetate and tartrate to normals and epileptics who had constantly acid feces and urine from intestinal fermentation. He found that in the non-epileptics the acidity rapidly disappeared, while, in the epileptics, it increased and sodium acetate and tartrate were found in the urine. Clinically, the epileptic attacks became more frequent and severe. Normally these salts should disappear by being transformed into carbon dioxid and water. In fact, these patients were made so much worse, that the entire experiment had to be discontinued. It seems proved that in epileptics there is a deficiency in the antitoxic alkalization function, as a result of which organic acids transformable into carbon dioxid and water, and which normally are oxidized into urea or sodium carbonate, are not so changed. The organism is constantly in need of sodium carbonate; absence of it quickly causes death by paralysis of the respiratory and vasomotor centers. Animals treated intravenously with hydrochloric acid and other acids will die in this way. The intestine is always alkaline, in contradistinction to the stomach, which is always acid. The formation of sodium carbonate, therefore, is vitally important, not only because the organism cannot live unless the blood and tissues are alkaline, but also because intestinal digestion, which is essentially the transformation of starch into maltose, cannot continue in an acid medium.

If acids or organic salts are not transformed into sodium carbonate, they enter the circulation, change the blood chemistry, and cause convulsions. Intravenous injections of acetic and hydrochloric acids or of sodium formate, acetate, butyrate, propionate and valerianate, cause convulsive attacks. The citrates and alkaline tartrates and other organic salts, produce severe convulsions when painted on the motor cortex. These organic salts, therefore, which are capable of causing convulsions, are precisely the ones which, in the epileptic, do not become transformed into sodium carbonate. Physiologists have never been able to locate exactly the organs in which this alkali-forming antitoxic process occurs. Cuneo studied in vitro the action of the intestinal mucosa on these salts, and used the pancreas, the liver and the bile. His conclusions, based on work done, are that this function of the transformation of organic salts into sodium carbonate begins in the mucosa of the intestines and is completed in the liver, whence the sodium carbonate is returned to the gut with the bile. He further noted that when the

content of sodium tartrate or acetate in contact with liver tissue was abundant, oxidization took place regularly and sodium carbonate was formed; but when these salts were present in small quantities, the reaction became acid because of a lack of bases. Much carbon dioxid developed and proteoses were found in the liquid under these circumstances. If the liver tissue was kept in contact with a 5 per cent. solution of sodium tartrate, the tissue remained unaltered for several days, the tartrate was transformed into carbonate, and other substances were found which he was able to identify as nucleinic acid compounds; these later, under certain conditions, became split into proteoses. But if the liver tissue was kept immersed in a physiologic saline solution, it changed rapidly and no nucleinic acid compounds or proteoses were found. Therefore, while sodium chloride is not capable of maintaining the activity of these ferments, sodium tartrate by means of the oxidization it undergoes, may not only favor this activity, but can also give rise to the formation of sodium carbonate. Because of this double function, these organic salts may not enter the circulation there, to manifest their toxic activities. To prove this point further, he introduced intravenously in dogs, solutions of sodium tartrate and acetate, and caused not only typical epileptic convulsions, but, immediately after the convulsions, he was able to recover from the carotid artery a substance which proved to be a proteose. He used the same research methods to identify this substance as when he first discovered the proteoses in the blood of epileptics.[11]

The problem is not clarified yet, however, because there is no explanation forthcoming from these experiments, as to the components of the blood which may, under certain conditions, liberate the substances which cause the convulsions, namely, the proteoses. Cuneo was able to produce convulsions in animals by the intravenous injections of proteose derived from nucleoproteins. Proteoses are not only developed in the intestines as a result of the metabolism of proteids, but may be obtained from that fundamental constituent of all cellular nuclei, nucleohistone. This substance is found in very large quantity in, and is easily obtained from leukocytes. It is very complex and contains an acid phosphorate, or nucleinic acid, and a basic substance or histone which has all the properties of a proteose. Nucleohistone under normal conditions, is a stable salt and is therefore innocuous; but, under special circumstances, this nucleoproteid divides into nucleinic acid and proteose, and the latter then manifests its toxic properties. Cuneo obtained this substance from leukocytes. He worked on the theory that these substances are produced by a process of oxidization. The blood serum was hydrolyzed and oxidized by a solution of hypochlorite of sodium. In this way, two substances were obtained which have the same chemical and biologic properties as nucleinic acid and

the proteoses. In an alkaline solution, these substances, one an acid and the other a base, remain united as nucleohistone, a salt. But, when the solution is made acid by the addition of acetic acid, with the formation of sodium acetate, a substance is precipitated which has all the properties of nucleinic acid. The most important indication of these is the ability to color the blood serum indigo blue with the resin of guiac. There remains in solution, however, a basic substance which has all the properties of the proteoses.

Cuneo studied the biologic effects of intravenous injection of these substances obtained from blood serum. He found that nucleinic acid is not toxic, but the basic substance (the proteose) causes typical convulsive epileptiform attacks in dogs. Animals dying in status epilepticus induced in this way, show the same pathologic changes in the viscera, brain, and their coverings, as do human beings who die from albumosemia (proteosemia).

He lists the necropsy findings in animals as follows: Hyperemia throughout all the viscera with many hemorrhagic infarcts; scattered pulmonary infarcts; infiltration of all tissues with bloody serum; vast edema; infiltration of the meninges, endocardium pleura and peritoneum; the presence of noncoagulable blood with the color of prune juice; distended gallbladder; and dilated heart. Tanzi and Lugaro[13] list the necropsy findings in human beings who died in status epilepticus, in practically the same way. The acute tissue change are: edema of the brain; hemorrhages and venous hyperemia in both the gray and white matter, but especially in the pia; frequent hemorrhages in the pons and bulb; acute changes in the cellular elements of the brain (swelling, chomatolysis, proliferation and swelling of neuroglia cells, and the presence of amoeboid glia cells); hypertrophy of the heart; hypoplasia of the large vessels; persistent thymus, etc.

In this connection, it is well to recall the work of Russell and the quotations from Sargent, which point to the vascular factor as important in the pathogenesis of the epileptic attack. The necropsy findings in human beings who died in status epilepticus show very definitely how severely the cardiovascular system is damaged. The necropsy findings in Cuneo's dogs dead from experimental proteosemia (albumosemia) were exactly similar, and, further, Cuneo points to the facts that the blood which he extracted from epileptics in status epilepticus, or immediately after severe convulsive seizures, was also of prune color and incoagulable, and contained proteoses.

Cuneo, therefore, believes that albumosemia exists in epilepsy. This is caused by an insufficiency of the alkali-forming function in the liver and the small intestine, by means of which the acid organic salts, which are transformable into sodium carbonate, do not undergo this metabolic

13. Tanzi and Lugaro: Mal. Ment. **2**:421, 1916.

change, but enter the circulation and cause a division, under certain conditions, of the nucleohistone element of the nucleoproteids into nucleinic acid and proteoses. These latter remain free and exhibit their convulsive action.

Based on this theory, Cuneo has recently made clinical therapeutic experiments. In order to aid the digestion of carbohydrates, he has attempted to administer alkali by mouth, but he readily admits the difficulties encountered. These are caused chiefly by the changes which these substances undergo in the acid content of the stomach. Remembering that the two substances obtained from blood serum are not split off in alkaline solution, but remain combined as an innocuous salt, whereas in an acid solution they decompose into the innocuous nucleinic acid and the toxic proteoses, he injected nucleinic acid in an alkaline solution subcutaneously, hoping thus to tie up the proteoses in the form of innocuous nucleohistone. Since 1917, when these therapeutic experiments were first begun, he has also ordered special diets restricted in the amount of carbohydrate (starches). This, combined with the alkali administration by mouth, has apparently given very encouraging results.

Before attempting to harmonize in a synthetic way the foregoing data, consideration must be given to the anatomic facts. These are best summarized by calling attention to the findings of Alzheimer [10] in cases of idiopathic epilepsy. His conclusions translated literally are:

> Macroscopically, a wrinkled, finely roughened condition of the surfaces of the convolutions, with more or less distinct sclerosis of the upper surfaces of the cortex. Microscopically, increase of the glia with a striking tendency to the preservation of the normal arrangement. There is also a considerable loss of nerve fibers and ganglion cells in the cortex. Many of the ganglion cells appear diminished in size, while others show certain changes, the specific significance of which must be further investigated. This cellular degeneration is spread over the entire cortex. There are reasons for believing that the nervous elements are primarily involved. The histologic changes indicate the presence of epileptic dementia.

Nissl, Bleuler and others (quoted by Tanzi and Lugaro) agree that these changes are more marked with the greater degrees of dementia. It must be kept in mind that all of the pathologic material was from old, demented epileptics. There has been of late a strong tendency to give to these findings no primary importance in the pathogenesis of dementia epileptica. It seems very probable that they are secondary and due to: the effects of the convulsive seizures; the prolonged toxemia which results from various attacks of status epilepticus; the effects of intracranial injury caused by the falls during attacks, etc. Many pathologists who have reported these changes, have seemed to stress the fact that they were most marked in the cornu ammonis. There is perhaps

nothing more significant in this observation than the clinically well-known fact that there is a type of hallucinatory epileptic seizure, often accompanied by convulsions, which has for its initial symptom a disturbance of the sense of smell or taste. A neoplastic or traumatic lesion in the rhinencephalon often gives rise to this type of seizure. As a general explanation for all the epilepsies, however, the localization of the gliosis and other pathologic changes in the cornu ammonis, has no more significance than the characteristic changes which occur in the same location in cases of senile dementia. No one has yet ventured to assert that all the mental phenomena of senile dementia are explained by the fact that the senile plaques and Alzheimer-Perusini neurofibrils [14] are found preponderatingly in the cornu ammonis and in the tips of the temporal lobes. It is of interest to note that in pure senile dementia, uncomplicated by the excessive, specific vascular and ectodermal changes of arteriosclerosis, the convulsive or epileptiform attack is rarely seen. Certainly, convulsion is not a prominent feature in the senile psychotic picture.

If we are to consider epilepsy as a disease of the brain, it is strange that there are not more local signs of brain damage in the clinical picture. In looking over fifty-seven private cases of epilepsy, which have been carefully examined neurologically a number of times, only three of them showed any objective neurologic sign of disease or injury of the nervous system.[15] Two of these were traumatic cases, and one was so-called idiopathic epilepsy. In the traumatic cases, there were definite signs of injury to the sensorimotor cortex. In the idiopathic case, there was a Babinski toe sign on the right, and a left external rectus palsy. These facts point away from actual brain change in any considerable proportion of cases of epilepsy.

A very brief mention of the bacteriologic theory of the pathogenesis of epilepsy is perhaps all that is merited. The idea that bacteria [16, 17] cause epilepsy has never proved more than a fanciful notion. The work of those who advanced this as a fact not only has never been confirmed,

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14. Bonfiglio, F.: Anatomia patologica delle psicosi dell' eta senile, Riv. sper. di freniat. **45**:219 (Jan. 31) 1922.

15. The question of aura in relation to "idiopathic epilepsy" has been held by many to stamp these cases as a definite entity distinct from other epilepsies. I was struck by the fact that many (twenty-four) of my private cases had no definite and constantly experienced aura at all, and all of the cases had some epileptic attacks without aura. The conception we advance explains the aura on the basis of stimulation, by toxic substances, of sensory areas shortly before the whole cortex is involved and unconsciousness supervenes.

16. Terhune, W. B.: A Bacillus Isolated from Epileptics, J. A. M. A. **67**: 1155 (Oct. 14) 1916.

17. Reed, C. A. L.: The Bacillus Epilepticus, J. A. M. A. **66**:1607 (May 20) 1916.

but Caro and Thom [18] disproved the claims almost as soon as they were made. Finally, it is important to consider the question of heredity and hereditary factors in idiopathic epilepsy. There are those [12] who believe with Pierre Marie that "the cause of epilepsy exists always outside the patient and operates prior to his conception." This implies that prenatal encephalitis, trauma, infection and intoxication, defective cardiovascular development, etc. are always operative in the causation of epilepsy. On the other hand, some authors are less definite, and incline to the belief that, in some sort of Mendelian manner, epilepsy is directly inherited as a recessive trait of the nervous system. However that may be, it remains undisputed that numerous statistical studies have failed to show anything definitely tending to substantiate these ideas. Grouping epilepsy with all other mental disorders, the search for hereditary stigmata has been successful in from 66.8 per cent by Dejerine (quoted by Tanzi and Lugaro) to 87 per cent. by Kraepelin. When epilepsy in the ascendants is considered alone in these studies, and a search is made for similar heredity, the results are disappointing, and even exhaustive statistical studies show how negligible this factor must be. Burr [19] has recently conducted such an investigation in a large series of cases with results which are barren for the notion that epilepsy is an hereditary trait in predestined individuals. Besides, no conception of the pathogenesis of epilepsy based on heredity alone, could possibly be made to explain all the epilepsies (traumatic Jacksonian attacks, general paralysis, arteriosclerosis, status thymicolymphaticus, brain tumor and cysts, alcoholism, etc.).

The sweeping statement of Pierre Marie, however it may fail to fit every case of epilepsy, does nevertheless explain a small group, especially the epilepsies of mentally defective and paralytic idiot children. His conception in these cases has undoubted validity. As with each of the theories of the pathogenesis of epilepsy above detailed, however, it leaves the subject as a whole, practically untouched. Not one of these conceptions, not even the vasoconstrictor vascular hypothesis of Sargent, or the biochemical explanation of Cuneo can be made to apply to all epilepsies.

Formulated briefly, our conception is that the research work of the future must be directed to the task of finding facts to substantiate and amplify the ideas of Cuneo. A defect in the alkalization function of the small intestine and liver in the process of carbohydrate metabolism, sets free in the blood toxic substances which, when they reach the

18. Caro, H., and Thom, D. A.: A Bacteriologic Study of the Blood of Seventy Epileptics with Especial Reference to the Bacillus Epilepticus of Reed, J. A. M. A. **67**:1088 (Oct. 7) 1916.

19. Burr, C. W.: Heredity in Epilepsy, Arch. Neurol. & Psychiat. **7**:721 (June) 1922.

brain, are capable of causing convulsions. In the idiopathic epilepsies, the proteoses or whatever the toxic substances may be, act on the larger cerebral vessels, as epinephrin or any acid does, and cause a sharp vasomotor disturbance with loss of consciousness. It will be recalled that proteoses like many other toxic substances, cause convulsions when painted on the motor cortex. With the large cerebral vessels constricted, the offending substance is imprisoned in the cortex and causes the generalized clonic convulsive phase of epilepsy. In the smaller attacks, the constricted area may be sharply circumscribed, as in urticaria or so-called angioneurotic edema. Thus we may explain the Jacksonian seizures. After a local vasoconstriction a transient hyperemia often follows, with transudation and the local liberation of toxic substances in the tissues. Lactic and other acids cause vasoconstriction in conditions of muscular exertion with diminished oxygen supply (asphyxia, violent exercise), or when injected intravenously.[8] In the brain, convulsions may be reproduced experimentally by painting the cortex with proteoses or other toxic substances. In the case of craniocerebral injury with scar adhesion, brain abscess, circumscribed areas of encephalitis, brain tumor, cysts, general paralysis, cerebral arteriosclerosis, etc., the toxic substance may be produced locally as a result of the vascular disturbances. Cuneo has shown that the breakdown of leukocytes and all cellular tissue releases the nucleohistone which decomposes under certain circumstances (acid mediums experimentally) into nucleinic acid and proteoses. Any cell deprived even momentarily of its blood supply may become acid. The local liberation of proteose in the cortex in all these conditions would again give this convulsion-producing substance an opportunity for activity. Disturbed vasomotor control locally, as an autonomic system defect, is an added possibility which must await definite proof. However, the smooth muscle of blood vessels has inherently a capacity to react to various substances by manifesting vasoconstriction or vasodilation. This may be caused by excessive nitrogen or carbon dioxid in the blood, as in asphyxia. In the spinal animal (cord divided below the medulla to remove the medullary influence on the vasomotor functions in the extremities) extensive vasoconstriction with spasm of the skeletal muscles occur and cause a marked rise of blood pressure when lactic and other acids are injected intravenously. Lactic acid is only one of a number of acids capable of producing this phenomenon.[8]

Starling [8] says in this connection that "in the absence of any direct histologic evidence of the existence of such centers (nerve centers in the walls of the vessels) it seems more rational to ascribe the tonus in peripheral blood vessels to the automatic activity of the muscular fibers themselves." The cerebral vessels in particular seem to be free from vasomotor control. This being so, the local liberation in an acid medium

(epileptic acidosis), or by the destruction of cellular tissue (leukocytes, ganglion and neuroglia cells, etc.), of nucleinic acid and proteoses will supply all of the conditions necessary for the production of the epileptic convulsion. The vasoconstriction might be caused by several toxic substances: proteose in so-called idiopathic epilepsy; epinephrin or some other substance in the so-called psychogenic (emotional factor) cases. In general paralysis and arteriosclerosis, the vascular disturbances and the local cellular destructive processes in the brain elements are ideally combined to produce generalized convulsive seizures. The periodicity of epileptic seizures in idiopathic cases would be explained by the occasional synchronous repetition of all the processes which produce the elements necessary to cause a seizure. The alkalization function may be sufficient to prevent the entrance of free organic acids or organic salts into the blood until the proper carbohydrate metabolic balance is upset, and causes an overwhelming acidosis and toxicosis, with the production of albumosemia (proteosemia). In cases where this condition obtains continuously for considerable periods, the status epilepticus supervenes or there is a fierce, sharp, mental epileptic equivalent or an even more prolonged and severe epileptic psychosis. No mental reaction is more severe, senseless, brutal or so apparently without reasonable basis, than the violent epileptic psychotic outbreak. The confusions[14] (aura) and deliria preceding or following even the ordinary epileptic attacks, are very similar to the toxic deliria or the deliria of toxi-infective exhaustive states. One, therefore, can make this conception satisfactorily fit all of the above marshalled data.

Regardless of whether the vasoconstriction or other vasomotor disturbance is caused by the adherent scar in a craniocerebral wound, by an acidosis, or by local disturbance of a theoretical autonomic vascular control of cerebral vessels, it must be remembered that brain cells particularly cannot long survive a cutting off from their blood supply. Even when this is momentary, catabolic changes begin to occur. In the breakdown which results if the cells are bathed in an acid medium, the nucleohistone breaks up into nucleinic acid and proteoses. The proteose then causes the convulsion. This is the explanation of such experiments as those of Pike.[9]

Therefore, the factor of importance in epilepsy is the acidosis, regardless whether this depends on a viciously functioning carbohydrate metabolism which causes a general toxicosis, or upon the local production of the toxic substance from disintegrating cellular structures, secondary to vascular disturbances. The effect is the same, the only difference is the extent of the convulsive reaction.

Obituary

ROBERT THAXTER EDES, M.D
1838-1923

Dr. Robert T. Edes died Jan. 12, 1923, at the home of his daughter in Springfield, Mass., at the age of 84. For many years he had not been closely identified with medicine because of advancing years and the infirmities dependent thereon, rather than through lack of abiding interest in his profession. Owing partly to increasing deafness, which rendered it quite impossible for him to attend meetings with satisfaction, or in fact to engage in the ordinary social relations of life, he was forced to retire largely from the interests which his active mind otherwise would have followed to the end.

Dr. Edes was born in Eastport, Me., Sept. 23, 1838. He was the son of a Unitarian clergyman and was descended from English stock, his ancestors having originally settled in Charlestown, Mass., toward the end of the seventeenth century. He was graduated from Harvard College in the class of 1858, and three years later took his degree in medicine at the Harvard Medical School. The Civil War had already begun at the time of his graduation and he forthwith entered the Navy, serving throughout the war and ultimately retiring with the rank of past assistant surgeon. During the four years of his association with the Navy he saw active service particularly in the engagements about New Orleans. Following this period, he undertook a course of study in Europe, and later settled in the neighborhood of Boston for the practice of his profession. He quickly took a prominent place among the physicians of that time and successively occupied the chairs of Materia Medica from 1875 to 1884, and of Clinical Medicine from 1884 to 1886, at the Harvard Medical School. He also held the post of visiting physician at the Boston City Hospital in a department, since abolished, of nervous and renal disease. During this period which was probably the happiest and most successful of his somewhat checkered career, he established a reputation for erudition and skill in diagnosis which was the envy of his contemporaries. While at the height of his success as a medical practitioner and consultant in Boston, he felt it necessary because of the illness of his wife to change his residence to Washington. This was in 1886, two years after his attainment of the professorship of Clinical Medicine at the Harvard Medical School. The conditions, however, were such that after a stay of about five years in Washington he returned to Boston and forthwith became

resident physician of the Adams Nervine Asylum in Jamaica Plain, a suburb of Boston, an institution established for the care of nervous conditions and, essentially, what we should now call "border-line" cases.

Dr. Edes, although versed in general medicine, and by no means a specialist in any narrow sense, nevertheless always took a very vital interest in disorders of the nervous system, both organic and functional, and became known as an authority for that time in this type of disorder. It was natural, therefore, that he should identify himself with organizations devoted to the special study of the nervous system. Although not one of the founders of the American Neurological Association, he became one of its earlier and most devoted members, resigning later when he found it impossible to take further active part in its deliberations. The Adams Nervine Asylum, a comparatively small hospital, did not offer full scope for the capacities of his really fertile and original mind. He remained at its head, however, for a number of years, practiced to a certain extent privately, later was a visiting physician to a sanatorium in Nashua, N H., and in 1903, moved to Reading, in the neighborhood of Boston, where he attempted to establish a small private sanitarium, particularly for nervous disorders. He was, however, through his deafness and through the progress of the years, losing somewhat his capacity to meet the exigencies of modern medical practice, so that after a period of waning success he retired completely from medical practice, and after a long period of semi-invalidism, which was the harder for him on account of his clear mental vision, he died at the ripe age of 84.

His life was rich in attainment; he had his share of the honors which his profession could bestow, but he was on the other hand saddened by various misfortunes of a personal sort. Among these stands out prominently the loss of his only son, Richard Edward Edes, a young man of great promise, who early in his career, at the age of 32, died after a lingering illness from tuberculosis. This son, educated at the Johns Hopkins University, the Harvard Medical School and Massachusetts General Hospital, was a man of exceptional attainment and promise. His death, coming at a time when his father had reached and perhaps somewhat passed the zenith of his career, was a blow from which he never recovered, which darkened the declining years of his life, but which he bore with characteristic equanimity and fortitude.

Dr. Edes had a large society membership, among the more important of which were the Association of American Physicians, the American Neurological Association, the Philosophical Society of Washington, the American Academy of Arts and Sciences and the American Medical Association. He was also a companion of the

Military Order of the Loyal Legion. He taught not only at the Harvard Medical School, but also, at different times, at Dartmouth on the subjects of Materia Medica and Therapeutics; while in Washington, he was a lecturer on diseases of the nervous system in Columbian University and at Georgetown University on renal disease. For many years an active member of the Massachusetts Medical Society, he was placed on the retired list in 1912. He was a ready and trenchant writer, and his papers and articles all bear the stamp of originality and clear thinking. Among his earliest ventures in the literary field was a paper written in 1868 on "The Part Taken by Nature and Time in the Cure of Disease," for which he was awarded a prize by the Massachusetts Medical Society. In this paper was foreshadowed his unwillingness to accept traditional views and generally accepted opinions, unless based upon most substantial foundations. He was always in the forefront of progress and often distinctly ahead of the thought of his time. For example, in this "dissertation," as it is called, the following passages occur: "The more philosophical spirit of modern inquiry, which leads us to look at things as they are, and not as we would have them to be, is causing scientific men to diminish their estimate of the physician's power over the natural processes of disease . . ." and further, "The medical profession of the present day, though possessing far greater knowledge of physiological and pathological science than ever before, and far greater resources in the arts of medicine and surgery, must yet be content to acknowledge the somewhat narrow limits of its curative powers, and while really doing much more, can honestly claim as its own work much less than earlier and less instructed generations thought they had a right to do." This was written fifty years ago and shows the healthy scepticism, since familiar enough, which, in the minds of the pioneers, was beginning to rouse the medical profession from its complacency. Dr. Edes' interest soon turned to the nervous system and there appeared from his pen, in a relatively short time, upwards of a dozen articles on brain tumors and about as many more on various other disorders of the nervous system. These, however, were interspersed with papers on anemia, cancer and renal disease, the latter, also, a subject in which he was vitally interested. His interest in physical therapeutics found expression in a handbook published in 1883 and later, in 1887, in a work on Therapeutics and Materia Medica. In 1885 he gave the Shattuck lecture before the Massachusetts Medical Society on "The New England Invalid." This, like his earlier paper, to which allusion has been made, foreshadowed with extraordinary perspicacity the modern trend in the treatment of the psychoneuroses. "The psychic element in invalidism is to be controlled by psychic means"; "Nervous invalidism is a psychosis, and the study of it is a branch of morbid

psychology." This lecture is a notable contribution to our knowledge of this complex field, written in a style of scientific exactitude and whimsical humor in rare combination. Up to the time of his death, although handicapped in other respects and perforce a recluse, his mind remained clear and he continued to write for various periodicals almost to the end.

Although buffeted by Fate more than most men and destined to drag out many years of his prolonged life in comparative inactivity, Dr. Edes stands out as a man distinguished among his fellows. Scientific ardor, a delightful sense of humor, geniality and clear mental vision were so happily united in him, that while recognizing his great accomplishment, one wonders what more he might have achieved had the circumstances of his life been more favorable. After his return from Washington in the early nineties he was unable to reestablish himself in a position commensurate with his sterling abilities. The world moved on and, in a material way, he was not able to keep pace with it, in spite of his intellectual acumen and unfailing interest in its progress. Few of his contemporaries are living, but, to the younger generation who knew him, his memory will be cherished as one of the outstanding figures of his time.

E. W. T.

News and Comment

AMERICAN NEUROLOGICAL ASSOCIATION

The forty-ninth annual meeting of the American Neurological Association will be held in Boston, May 31, June 1 and 2, 1923.

AMERICAN PSYCHIATRIC ASSOCIATION

The annual meeting of the American Psychiatric Association will be held June 19 to 22, 1923, inclusive, at Hotel Statler, Detroit, Mich.

Abstracts from Current Literature

SPIROCHETES IN THE CENTRAL NERVOUS SYSTEM IN GENERAL PARALYSIS. F. JAHNEL, Ztschr. f. d. ges. Neurol. u. Psychiat. **73**:310, 1921.

Jahnel begins with a summary of the findings of Valente, a Portuguese investigator, who made brain punctures on cases of general paralysis after the method of Forster and Tomasczewski. He found spirochetes in 70 per cent. of the cases. In several he found spirochetes only after a second puncture, thereby proving that failure to demonstrate spirochetes does not prove their absence. There was no relationship between the finding of spirochetes and the stage of the infection, the duration of the paralysis, or the clinical form. In three cases he found spirochetes although the spinal fluid gave a negative Wassermann reaction; in four cases the Wassermann test was doubtful and twenty-one times it was positive. There were no morphologic or staining peculiarities of the spirochetes. The histologic examination in these cases gave a typical picture of general paralysis. In one case the spirochetes were extraordinarily numerous; they were never found in the pia, were numerous in the molecular layer and present even in the membrana limitans. The spirochetes were found in largest numbers in the second and third cortical layers. They were only rarely found in the white substance. In the neighborhood of the spirochetes, Valente found marked cell loss and a considerable new growth of vessels. Nevertheless, in some places with most marked tissue change, there were relatively few spirochetes. Valente believed that the organisms were not equally distributed throughout, but that in different places there were groups of spirochetes. Contrary to the findings of Noguchi, Valente demonstrated spirochetes in the neighborhood of the vessels and lymph sheaths, at times even in the lymph sheaths of the large vessels which enter the brain substance from the pia. Valente never found spirochetes within the plasma cells, although he found them between plasma cells. Groups of spirochetes were also present around the ganglion cells. He attempted to infect rabbits with puncture material from living general paralytics as well as with blood and spinal fluid; but in spite of many attempts in 103 animals he had only negative results. (In the clinic of the reviewer negative results were also obtained.) Valente concluded, as had Forster and Tomasczewski, that the virulence of spirochetes from general paralytics was reduced for the rabbit. He considered the paralytic process as the product of local spirochetal effects in the central nervous system. He inclined to the opinion that general paralysis develops from the early syphilitic meningitis, and that the spirochetes, in some manner still unknown, break through the limiting glial membrane.

Jahnel says that every variety of spirochetal finding in the brain of syphilitics is possible. Sometimes they are present in large numbers; sometimes only in a few places; sometimes in many areas throughout the brain. Cases in which one can find many spirochetes in the brain are relatively rare. Still they can be found in a great many cases, probably at least 50 per cent. In brain punctures, Forster and Tomasczewski found spirochetes in 47 per cent. and Valente in 70 per cent. In those cases in which they were not found one

must remember that the whole brain was not searched. In those cases in which death follows a paralytic attack they are usually found. He states that Ehrlich advanced the theory that the spirochetes in general paralysis have an increased resistance due to the fact that, after invasion, antibodies are formed which kill all but the resistant spirochetes. There thus arises a strain with increased resistance, which will again call forth more antibody formation and again kill all but the resistant ones, and so on ad infinitum. However, there is no proof of the validity of this theory. Jahnel then presents the theory of a neurotropic strain and calls attention to the work of Levaditi and Marie. Jahnel is not quite ready to accept their views, and among other things calls attention to the fact that there is a form of rabbit spirochetosis which may at times occur and thus spoil the value of the experiment.

He calls attention to the great rarity with which spirochetes have been found in the internal organs of adult syphilitics as contrasted with congenital syphilitics. The work of Warthin in finding spirochetes in a large number of cases is novel. Jahnel himself says he has searched through the internal organs of a number of general paralytics without finding spirochetes. Once he found spirochetes in the lung, and thinks they may have made their way there from the brain. He also found spirochetes in the aorta and presents a photomicrograph of them.

He agrees with Noguchi that in general paralysis spirochetes are found chiefly in the cortex of the brain. He has occasionally, though rarely, found them in the white substance. In the cortex the spirochetes are generally located in those areas in which the general paralytic process is recognized to be most frequent. They are found most frequently in the region of the frontal pole. However, they are also to be seen in the central convolutions, in the temporal, parietal, and, least frequently, in the occipital region. He has also found them in the optic thalamus, in the cerebellum, and in the midbrain, which is of interest in relation to the pupillary abnormalities which are so common in general paralysis. He states that there is a very great difference in the number of spirochetes to be found in different brains. He feels that there are some brains in which long search will not reveal spirochetes. There are others in which they are present in very great numbers. This does not agree with the uniformity of the findings in the cerebrospinal fluid, and leads Jahnel to believe that there may be a different form of spirochete.

Jahnel says that he has found spirochetes in places where they had not previously been found; in the meninges of the cerebellum, in the midbrain, in the walls of the basillar vessels and in several cerebellar veins. Generally, however, the spirochetes are found only in a few places. The spirochetes have only been found in the meninges occasionally; frequently in large numbers in the cortex. However, whenever Jahnel found spirochetes in the cerebellum he also found them in the meninges of the cerebellum. The question as to whether the cases in which spirochetes were found in the meninges might not be cases of cerebral syphilis rather than general paralysis is answered by Jahnel in the negative as the result of his microscopic examinations. It is to be remembered that in cases of true brain syphilis the spirochetes are present in very great numbers in the meninges as contrasted to a few in those cases of general paralysis in which they have been found at all. The finding of spirochetes in the meninges in cases of general paralysis makes a bridge between the cases of cerebral syphilis and general paralysis, and perhaps helps us in the question of preparalytic conditions and in the

therapy of general paralysis by showing that the battle must be not only against the spirochetes in the brain substance but also against those in the brain membranes.

As regards tabes, the finding of spirochetes is much more infrequent than in cases of general paralysis. Noguchi in his original study of twelve cases found only a few spirochetes in the posterior column of one case. Shortly after, Versé reported two cases of tabes in which spirochetes had been found; in one case they were in a posterior root; in the other case in a spinal ganglion; but he was not entirely sure that the objects seen were really spirochetes. Then Richter in a profound study of the histogenesis of tabes stated that the real point of attack was the nerve of Nageotte. He found spirochetes in the granulation tissue of the posterior root. Jahnel says that in many searches in the past he was unable to find spirochetes in the spinal cord, either in tabes or general paralysis, but more recently, when he made sections with the dura intact, he found spirochetes in the arachnoid tissue in different places, at times in groups, at times singly. He also found them in the membranes of the posterior root. He thinks that in removing the dura in the past, a good deal of the arachnoid tissue was torn away, and this accounts for having missed them. In considering the relationship between the finding of spirochetes in tabes and the pathogenesis of the disease as regards localization, it must be remembered that the anatomic preparations show the end-result of the process that has lasted for years, whereas the spirochete finding represents a condition that obtained at the moment of the death of the patient.

As to the spatial arrangement of spirochetes in the brain, Valente believes that they are more likely to be found at the base of the convolutions than at the top. They occur at times in small colonies in the center of which is a brown colorization, the cause of which is not clear. Another interesting condition is the presence of spirochetes in relation to the blood vessels. Jahnel thinks that this latter is more in the nature of colony formation. The finding of spirochetes in the vessel lumen, Jahnel considers to be the result of postmortem change; they have never been seen in the blood channels during life. The question of spirochetes in the spinal fluid is also in doubt. It is possible that when found as the result of animal inoculation they may have been forced into the fluid, and were not really growing there. In the brain cortex the spirochetes, in the majority of instances, are in the nerve cell layers and only rarely do they occur in the molecular layers. A relationship to certain tissue elements has not been proved. Occasionally, one finds ganglion cells surrounded by a number of spirochetes. The presence of spirochetes within the ganglion cell has been but rarely reported and is not certain. Jahnel feels that this is a matter of subjective interpretation; the same is true for the relation to glia cells.

This article is very well illustrated with photomicrographs which demonstrate the presence of spirochetes in the various portions of the brain. This work on spirochetosis in the brain of general paralytics is opening new channels for the study of the etiology and pathogenesis of general paralysis. The same is true for tabes. As a result of the improvement in staining technic for spirochetes which has been devised by Jahnel, great progress in this study has been made in the last two or three years, especially by Jahnel and his students Hermel and Jacob. In this country Dunlap has contributed a most interesting and valuable review in an article which was published in the ARCHIVES, December, 1922, page 589.

SOLOMON, Boston.

CLINICAL CONSIDERATIONS ON PARKINSON'S DISEASE FOLLOWING ENCEPHALITIS. G. CATOLA, Riv. d. Patol. nerv. e ment. **27**:62, 1922.

The author believes that the Parkinsonian syndromes of epidemic encephalitis belong fundamentally with genuine Parkinson's disease. This conclusion is of great clinical importance as it implies the existence of an intimate relation of cause and effect between an infection, encephalitis, and paralysis agitans, and thus throws a bright light on the hitherto obscure and controversial problem of the etiology and pathology of this disease. Until now the most frequent causes of Parkinson's disease were stated to be trauma, acute and prolonged emotions, and cerebral arteriosclerosis; only a few authors have sought to connect this condition with various infections or intoxications. Of these the most frequently mentioned were plumbism, acute articular rheumatism, scarlet fever, typhoid and dysentery. Dana, in 1898, was the most insistent upholder of the idea that infections and intoxications were the cause of the condition regardless of whether they had existed a longer or a shorter time prior to the onset. The author very strongly disagrees with the idea that even grave trauma or emotion, no matter how violent or prolonged, have any etiologic or pathogenic influence on the production of the Parkinsonian syndrome.

It is only necessary to call upon the evidence accruing from the late war, with the immense numbers of severe organic and functional nervous system injuries, and to note that there has not been as a result an exceptional or even noteworthy increase in the number of Parkinsonian cases. The author believes that any increase of these cases caused by intense prolonged emotional stress or actual injury to the nervous system following the war would have been commented upon. The author feels that the histories cited by those who have reported Parkinsonian cases following trauma or emotional stress, do not stand critical analysis well. Besides, he fails to understand how a physical or psychic trauma can, of itself, induce anatomic lesions which have a chronic and progressive evolution which presupposes the continuous action of an agent over a long period. The notion that Parkinson's disease is caused by precocious, senile or arteriosclerotic changes in the nervous system, is not borne out by the presence of this condition in young children and youthful individuals.

The author refers to the cases of Ramsey Hunt, who separated a definite group of juvenile cases from the presenile and senile types, and placed them on a definite autonomic and pathologic basis. The author does not believe that Parkinson's disease has a different etiology from that syndrome following any infection which involves the corpus striatum and the locus niger. Any disease process operating in the area of the brain where modern research has placed the localization of the anatomical changes in Parkinson's disease, will give origin to a similar picture. In other words, it is necessary to determine whether Parkinson's disease is a syndrome depending on the presence in the same area of many diverse processes or whether it is a nosological entity always due to one cause. Eliminating those very rare cases caused by gross lesions such as tumors, softenings, cysts, etc., it is possible to sustain a theory that this condition is universally of an infectious origin.

The anatomic and pathologic investigations of Hunt, Tretiakoff, Souques, and others, have revealed that there are always demonstrable histologic lesions to be found in the striomesencephalic region. This part of the brain may be said to have a special affinity for many varieties of toxi-infections. However, this hypothesis does not appeal to the author because of the relative rarity of Parkinson's disease, as compared with the frequency of the infections and intoxications. Others advance the theory that the special vulnerability of this

region is congenital or acquired thus making for a locus of less resistance to varied types of infections. This supposition would have great weight if there existed a more obviously direct relation of cause and effect between the development of Parkinson's disease and those infections which it has been held might be the cause of the condition. In looking over the histories of these cases, analysis fails to show an intimate and immediate connection. The author was surprised to find that the presumed causal infection had occurred at a time so remote that it was impossible to consider that any etiologic connection existed. He further observes that if the peculiar predilection as to the site of the disease were conditioned by exaggerated vulnerability due to pre-existing causes, it would be impossible to explain the percental difference in the occurrence of Parkinson's disease following infections in general and encephalitis in particular. The statistics of Barré and Reys show twenty Parkinsonian cases out of a total of one hundred and one cases of encephalitis.

The author stresses the point that it is exceptional to find an obvious connection between Parkinson's and any other infectious disease. He believes that it is logical to ascribe an elective localization to the virus of encephalitis and that, as a result, the pre-eminent infective etiologic cause of Parkinson's disease is always similar. The frequency of Parkinson's syndrome in epidemic encephalitis is compared to the epidemics of poliomyelitis, while the sporadic case of Parkinson's is comparable to the occasionally encountered case of Heine-Medin's disease in endemic form.

The author calls attention to the experience, which he shares with many others, that many Parkinsonian cases have followed *formes frustes* of encephalitis; some of these cases have been afebrile and ambulatory and the diagnosis was first made when the Parkinsonian features were noted. He feels that there is a strong connection between these attenuated types of encephalitis and the ordinary Parkinsonian picture. In fact, many months often intervene between the abortive atack of encephalitis and the onset of the Parkinsonian picture. The author also stresses the findings of Barré in 1910. This author found that many classical types of Parkinson's disease have shown weaknesses of the ocular muscles and diplopia. The author concludes that there does not exist any difference between the classical Parkinsonian syndrome and that following encephalitis and that the same infection may always constitute the direct cause of this picture. The isolated so-called classical types are caused by sporadic *formes frustes* of encephalitis epidemica.

This article was part of a symposium on encephalitis and was read at the annual congress of the Italian Neurological Society which was held at Florence, Oct. 19, 1921. It was also read at the reunion of the Neurological Society of Paris, June 1, 1921. At the Paris meeting the author's opinions were endorsed by Souques and other Frenchmen. He stresses the progressive, chronic, incurable nature of the postencephalitic Parkinsonian cases.

OSNATO, New York.

REVIEW OF THE CLINICAL SEQUELAE OF THE RECENT EPIDEMIC OF LETHARGIC ENCEPHALITIS. F. NAVILLE, Schweizer Arch. f. Neurol. u. Psychiat. **11**:34, 1922.

The most frequent and important sequelae of encephalitis are the development of the Parkinson syndrome, pains, myoclonias, disturbances of sleep, and mental enfeeblement. Naville, in reviewing the history of the disease, states that in 1915, 1916, and 1917 Cruchet and Economo recognized an epidemic of encephalitis, which the former called subacute encephalomyelitis and the latter, encephalitis lethargica. In 1918 a form with predominence of medullary

symptoms appeared in Australia, also the myoclonic and Parkinson types. The epidemic subsided in the summer of 1920 only to reappear in the first months of 1921.

The incidence in Switzerland was 0.3 per ten thousand. It did not affect the urban population predominantly as in highly contagious epidemics. The greatest incidence was in people between the ages of fifteen and fifty years, although infants and people of eighty years of age were stricken. The mortality was 20 per cent.

Preceding epidemics had been reported by Hildestein in 1695 as sleeping sickness; in Tübingen, in 1713; as Dubini's chorea in 1846; by Gayet in 1875; and as nona in 1890. Little more has been learned conerning recurrences, chronicity, delayed exitus, and subsequent aggravation of symptoms than was known at that time.

In reviewing the symptomatology, Naville discusses diurnal somnolence, amnesias, sexual frigidity, apathy, syncope, vertigo, Parkinson states, insomnia, pains, chronic headache, visual disturbances, mental deterioration, general feebleness, fatigue, salivation, decrease or increase of appetite, obesity, modification of the genitals, and ocular disturbances. Grossmann, who followed a hundred cases of encephalitis from six to seventeen months after the acute attack, found a persistence of psychic disorders, as neurasthenia and hysteria, in 55 per cent.; involuntary muscular movements and tremors in 58 per cent.; disturbance of muscle tonicity in 18 per cent.; residual cranial nerve palsies in 64 per cent.; pupillary abnormalities in 30 per cent.

The Parkinson syndrome may develop after any type of onset. As a rule it begins within the first two months, but it may appear very insidiously many months after recovery seems to have been complete. The author reviews the various explanations advanced for the development of this syndrome, including emotional disturbances, muscular lesions, endocrine disorders, lesions of the locus niger, degeneration of the striothalamic fibers and of the ansa lenticularis, lesions in the globus pallidus and the efferent fibers in the body of Luys. Recent investigations seem to point to constant involvement of the locus niger, both in the classical Parkinson's disease and in the post-encephalitis Parkinson syndrome. Numerous theories regarding the physiopathology of these muscular disorders have been erected and are reviewed by the author. There seems to be no agreement.

In discussing the pains that sometimes accompany this illness Naville cites various views regarding their probable origin. In some cases pains appear to be radicular, in some sympathetic, in some meningeal, and in others medullary. They may appear in any part of the body, are often mobile, and may or may not be associated with muscular phenomena.

Acute chorea and generalized locomotor excitation and delirium have been common at the onset. Choreiform, clonic, rhythmic, fascicular, and ameboid movements are among some of the later manifestations of involuntary muscle movements. These movements may be continuous or may recur at more or less regular intervals, such as the *crises quotidiennes* of Harvier. On the whole, myoclonic movements present in the same individual are synchronous. Marie has called particular attention to simultaneous flexion or extension of a leg with coincident adduction of the arm and elevation of the shoulder on the same side under the euphemism *chorée salutante rythmique.* The maximum duration of these movements is not known. They seem to diminish in intensity, in amplitude, in frequency, and then disappear during sleep. They may resemble functional disturbances. On the whole their prognosis is more favorable than

that of the Parkinson condition. It seems that the former are irritative phenomena while the latter is based on a definite atrophic lesion. Sometimes a progressive cachexia with mental disturbance may supervene.

An interesting type of encephalomyelitis, in which myoclonic phenomena may appear, has been described in dogs. There are found diffuse vascular lesions in the cortex, brain, bulb, cord, and meninges. Chauveau has shown that if different sections of the cord of such an animal are made, each segment will continue to produce its own set of movements independently. This segmental explanation, however, will not cover all cases, particularly those in which there may be synchronous movements of one side of the face and of the opposite arm and leg. Some authors insist that all of these disturbances arise in the basal ganglions. Thomas has described a very instructive case in which these movements were synchronous with the cardiac pulsation. The fact that patients having the Parkinson syndrome sometimes complain of a subjective tremor which can not be seen objectively, has led to the hypothesis that these disturbances may have their origin on the sensory, rather than on the motor side.

The mental sequelae are very interesting and a paper on the subject by Naville has been published in L'Encéphale, June and July, 1922. In spite of the frequency of initial delirium, true psychoses which are prolonged do not often develop. Naville thinks there is something rather characteristic both in the initial delirium, often present without pyrexia, and in the later psychoses. In these he recognizes a characteristic lethargy, or psychomotor torpor. This raises the interesting question as to what component of this psychomotor torpor is physiologic and what psychologic. The question is a large one and has a bearing not only on this, but on other psychiatric problems as well, such as the influence of tics, choreas, professional cramps, psychomotor obsessions, psychasthenias, etc. He proposes the name *bradyphrénie* for this characteristic post-encephalitic mental state, so often present without Parkinsonian rigidity.

Delayed deaths are occasionally due to progressive cachexia in the Parkinson and in the myoclonic types, bulbar accidents, intercurrent diseases, and finally recurrences of the disease itself.

WOLTMAN, Rochester, Minn.

GENERAL PROTEIN THERAPY AND ACTIVE IMMUNIZATION OF GENERAL PARALYSIS. W. JACOBI, Ztschr. f. d. ges. Neurol. u. Psychiat. **73**:575, 1921.

Jacobi outlines an attempt to treat general paresis by the process of developing an active immunity toward the spirochete. He develops his theory as follows: at the time when specific chemotherapy for the so-called metasyphilitic conditions was forsaken (prior to the arsphenamin era) one recognized the occurrence of spontaneous remissions in general paralysis which, although occasional, were still a definite indication that a protective reaction (Abwehrreaktion) occurred which apparently brought the disease process to a standstill for the time being. The work of Gennerich has caused interest again to turn to immunity processes in the metasyphilitic diseases. According to Gennerich the development of these conditions has the closest relationship with the healing of the infection in the cerebrospinal fluid. The more generalized throughout the body the infection with the organism, the greater the production of immune bodies and hence the greater the probability of resisting the infection. The severe skin lesions in the beginning of the disease in many syphilitics are an expression of the increased resistance of the body in the sense of an allegeric reaction, which apparently has a great relation to the later development of metasyphilis. Those cases which had marked skin lesions

very rarely develop tabes or general paralysis. If the protective reaction (Abwehrreaktion) is weak, some strains of spirochetes will remain behind in those places where the protective mechanism is especially poorly developed. According to Gennerich's view, this is especially true of the meninges. He believes that the course of the fluid infection is inversely proportional to the extent of generalization of the process, and that here lies the danger of antisyphilitic treatment, especially with arsphenamin. When most, but not all, of the organisms are killed by arsphenamin, and the natural immunity is thereby reduced, there is danger of greater growth of the organisms unhindered by specific antibodies. In the majority of cases there is invasion of the central nervous system during the primary and secondary stages. Thus they are prepared for later manifestations.

Jacobi calls attention to the skin reactions which are produced in syphilitic persons by injection of syphilitic organ extracts. This "allergic serum reaction" occurs in gummatous lesions and in congenital syphilis but not in the metasyphilitic conditions. The appearance of this reaction tends to show that the infected person has a strong protective reaction. The failure of the skin reaction in the case of general paralysis leads Jacobi to deduce that the protective mechanism is lessened in this condition. He therefore assumes that, in these metasyphilitic conditions, which are after all active syphilis, there is reason to activate the immune responses. The fact that remissions occur indicates to him that it is possible for such immunity reactions to occur spontaneously. In regard to this reaction he uses the method for producing active immunity, namely injection of syphilitic material. For this purpose he used extracts of syphilitic fetal liver. Similar vaccine treatment has been tried in other stages of syphilis with varying result; some investigators believe that good results were obtained; others that the method was worthless. Jacobi made injections of extracts of syphilitic fetal liver in increasing doses in three patients. The first patient received 59 c.c. of the extract in forty-three injections. The second patient 55 c.c. in thirty-seven injections and the third patient 50 c.c. in thirty-eight injections. Febrile reactions and chills followed the injections. The first patient treated, aged 48 years, had an expansive type of general paralysis. There was no effect upon the serology, the psychosis became more marked, and he died about six months after the commencement of the treatment. The second patient, 49 years of age, had also an expansive type of general paralysis. The Nonne-Appelt reaction became negative, the cell count was reduced, and the spinal fluid Wassermann reaction became weaker. The patient improved and was able to go home. The third patient, aged 37 years, presented a simple dementing type of general paralysis. In this case, the Nonne-Appelt reaction became weaker, the cell count decreased and the man also developed a remission.

In summarizing the results of his half-year of experience in the treatment of these three cases, with remissions in two, Jacobi questions the reason for this result. If it is to be assumed that the remissions were the result of the treatment there still remains the question whether it was a specific or nonspecific effect of the treatment. Recalling the results which have been claimed for non-specific protein therapy and infectious fevers as reported by Wagner-Jauregg, Döllken, Donath, Plaut, Steiner and others, Jacobi admits that his results may have been caused by the febrile reaction rather than as a specific reaction to the syphilitic extract. However, he feels that it is theoretically possible that the results may be due to the combination of a specific immunity with the effects of fever and leukocytosis.

SOLOMON, Boston.

A CASE OF CONGENITAL MEGACOLON (HIRSCHSPRUNG'S DISEASE) ASSOCIATED WITH MENTAL DISORDER AND TERMINAL CEREBELLAR HEMORRHAGE. N. D. C. Lewis, J. Nerv. & Ment. Dis. **56**:193 (Sept.) 1922.

The patient was of Scandinavian race. The father was an alcoholic, and a brother and sister died of tuberculosis. At 15 the patient began to drink and continued the excessive use of alcohol for several years. At 23 he had typhoid fever and a short time later, while intoxicated, a homosexual experience. At the age of 27 he was imprisoned on a charge of train robbery, and after six or eight years was transferred to the government hospital because of insanity. The striking mental symptoms noted there were: auditory, visual, and gustatory hallucinations; delusions of persecution, and emotional indifference. At times he assumed peculiar attitudes and was then negativistic. The principal physical manifestations were epileptiform seizures and recurrent attacks of acute abdominal distention with visible peristalsis. During one of these latter attacks the patient died with manifestations of shock.

At necropsy the colon was found to be enormously dilated. Macroscopically, the liver and spleen showed interstitial changes. Acute and productive changes were noted in the kidneys. The right testicle was not found. There was a chronic interstitial myocarditis with hypertrophy of the left auricular appendage, some sclerosis of the aortic valve and of the arch of the aorta and terminal pulmonary congestion. The brain weighed 1,470 grams. The dura was slightly adherent to the pia; congestion and arteriosclerosis were present. There was a hemorrhage in the right lobe of the cerebellum which had destroyed the central cerebellar substance. Microscopically, the pituitary showed sclerosis with compensatory hypertrophy; the thyroid showed diminution of colloid and acini; the adrenals exhibited deficiency in the development of the cortex and hypoplasia of the medulla. The principal changes in the cerebral cortex were arteriosclerotic processes. The hypertrophied wall of the intestine showed an enormous increase of the inner and outer muscular bundles with fibrous and arteriosclerotic changes in the submucosa.

In his analysis of the case the author offers explanations for the patient's behavior which are based on the pathologic changes. Thus, a delusion that there were many people in the abdomen is explained by the sensations which arose from chronic abdominal distension; fears are explained by pressure on the thoracic organs.

Vonderahe, Philadelphia.

SEVERE CHANGES IN THE NUCLEI OF THE GANGLION CELLS IN A CASE OF DEMENTIA PRAECOX. Arnold Stocker, Ztschr. f. d. ges. Neurol. u. Psychiat. **75**:47, 1922.

Stocker presents his discovery of marked changes in the ganglion cells of the brain from a case diagnosed as dementia praecox. The brain was from a woman aged 35 years, who was married, and the mother of three living children aged 8, 9 and 10 years, respectively. Five or six years before death she had a very difficult confinement and gave birth to twins; one of them was stillborn, the other died shortly after birth. The woman was ill for eight weeks at that time. In July, 1918, fifteen months before her death, the relatives noticed a change in her character. She angered easily, tired with her household duties and wished to be alone. Her speech was often inappropriate. At times she did not sleep and took hardly any nourishment. In this condition on several occasions she left home. At times she became very

angry and quite disturbed; at other times she was quiet and refused to talk. Finally she was committed to a hospital. At first she remained quietly in bed, kept her head under the covers, and only exceptionally made some small voluntary movement. She resisted the removal of the covers and buried her head in her breast. Memory and orientation were well preserved. After a time she became mute, and slept well, but it was difficult to feed her. Physical examination revealed cyanosis of the extremities and fleeting edema of the lower limbs. The reflexes were normal. She died in April, 1921, with symptoms of enteritis, but without fever. At necropsy the brain appeared normal macroscopically.

Histologically, however, the author found many cell changes. Examinations were made and descriptions are given of the following areas: the right and left second frontal; left first temporal; left and right caudate nucleus; left and right first frontal; left globus pallidus; left putamen; right thalamus; left subthalamic region; right locus niger; the medulla oblongata, and the cerebellum. In all these regions pathologic changes of considerable extent were found. Among the changes described, most weight is laid upon the presence of conglomerations of well stained, fine granules within the nuclei of the ganglion cells. In all regions examined, without exception, there were definite degrees of disorder of the ganglion cell protoplasm. As paradigms of the histological findings Stocker mentions the following: Among ganglion cells with high grade of chromatolysis, in which the cell protoplasm often stained very lightly and showed a vacuolated structure, neuronophagia and proliferation of the glia tissue were present. Many of the ganglion cells showed chromatophilia; often the cell structure was homogeneous so that cell protoplasm, nucleus and nucleolus could not be distinguished. Within the nucleus the granules already mentioned were deeply stained and of various sizes. Many of the ganglion cells contained considerable amounts of pigment as well as lipoid bodies. Pigmentation and lipoid bodies were also found in some of the glia cells and granule cells (körnchenzellen) of the vessel wall.

Ten cell pictures accompany the article. Stocker concludes by saying that he considers the ganglion cell which is described as an intermediate stage between the normal nuclear structure and the frequently described gray homogenization of the cell nuclei. He states that this finding is by no means pathognomonic for schizophrenia but that it is found in other pathologic brain processes; in fact he states that he has seen the same condition in epidemic encephalitis.

SOLOMON, Boston.

CLINICAL PICTURE AND PROGNOSIS OF THE FREQUENT MINOR FITS OF CHILDREN. E. STIER, Ztschr. f. d. ges. Neurol. u. Psychiat. **80**:143, 1922.

Pyknolepsy is the term used by the author to denote the convulsions which occur in infants or children, and which are not really epileptic in nature. He traces the subsequent history of a number of such cases in some detail and classifies them for prognosis according to the clinical manifestations. Certain characteristics, he says, will point one way or the other.

"The prognosis is absolutely good only when the attacks begin between the ages of 4 and 12. The children in question come only occasionally from families in which alcoholism, epilepsy or psychoses are present. The children themselves are not always free from intellectual backwardness, and occasionally have been subject to spasmophilia, to attacks of holding the breath or to tantrums. These features have no influence on the prognosis.

"The attacks commence out of a clear sky and without any previous excitement. The course is usually, but not always stereotyped until after months or even years, the attacks may cease abruptly, or much less often gradually, without leaving any residual nervous or psychic disturbance. Even with persistence of the attacks after puberty, the prognosis may be good.

"Symptomatically, the attacks are characterized by sudden and short interruption of the higher psychic processes, and by the monotony of the course. Enuresis, rigidity of pupils, slight raising of the arms, and slight, though not convulsive, rotation of the eyes and head are frequently present. On the other hand, deep loss of consciousness, injury in falling, running into objects, partial tonic or clonic convulsions, even when very mild, fear, palpitation or other vasomotor symptoms, and the occurrence of attacks during sleep, are always suspicious and are hardly consistent with a good prognosis.

"Onset of the attacks before the fifth year, fatigue or disorientation immediately after the attack, and control of the attacks by luminal are features which speak against the diagnosis of pyknolepsy and therefore against a good prognosis. It is unlikely that these attacks will resemble psychic fatigue or narcolepsy in the sense of Gélineau.

"On the whole we have in pyknolepsy a disease picture the etiology of which is quite obscure, but which presents a fairly definite symptom complex, and which can always be clearly differentiated from epilepsy."

FREEMAN, Philadelphia.

MANIFESTATIONS OF THE FEMALE CASTRATION COMPLEX. KARL ABRAHAM, Internat. J. of Psychoanal. **3**:1 (March) 1922.

Abraham summarizes and elaborates herein a frequently discussed but unclear concept of psychanalysis. This concerns the wish of many women that they had been born male instead of female. He holds that this wish is manifested both in conscious and unconscious aspects and in multiform ways. The repressed envy of the male sex is shown particularly well in the dreams and symptoms of some psychoneurotic patients. Abraham first disposes of the rationalizations for the renunciation of the female sex, often offered by these women, such as deprivation of business and social privileges, disfranchisement, etc. He then declares that psychanalysis has repeatedly discovered that, at certain stages of their development, little girls feel at a disadvantage as compared with boys because of their poverty in external genitals; they are envious of the penis. Although primarily without a feeling of inferiority, because she believes that all children are formed like herself, when the little girl learns the truth she may fabricate a theory that she too was once like a boy, but that, for reasons which are usually punitive, her penis has been taken away and has left a wound, the vulva. This theory is later reinforced by the flow of blood from the wound.

This discovery injures the girl's *amour propre;* it stimulates a sense of inferiority with a compensatory feeling of hostility, and impulse to rob. Abraham links with this the data of Freud's "Das Tabu der Virginität," the theory of the right of the first night, and the savage custom of defloration by a priest or friend. This feeling of envy and desire for revenge may be manifested in various ways, such as a marked interest in crippled men, in bald headed men and the like. It is compensated for symbolically in many women by the assumption of masculine habits and manners; in a less sublimated form it is replaced by an interest in the feces (overt and sublimated anal eroticism) because feces are parts of the body which are lost, and symbolize the penis.

Unadjusted repression of these so-called castration wishes may later lead to the dread of marriage, marital discord, frigidity and the well known phobias of wounds, knives and cutting.

Abraham illustrates his findings liberally, and introduces connotations which are not mentioned in this abstract. He concludes with a paragraph worthy of quotation, partly because of its intrinsic worth and partly because it takes up a matter very generally misunderstood by the antagonists of psychanalysis: "To everyone of us who practices psychanalysis the question occurs at times whether the trifling number of individuals to whom we can give assistance justifies the great expenditure of time, labor and patience. The answer to this question is contained in the above exposition. If we succeed in freeing such a person from the defects of her psychosexuality, i. e., from the burdens of her castration complex, then we obviate the neuroses of children to a great extent, and thus help the coming generation. (Because women whose ideas and feelings are influenced by the castration complex to an important degree, whether consciously or unconsciously, transplant the effects of this into their children.) Our psychanalytic activity is a quiet and little recognized work, and for this reason all the more attacked, but its effect on and beyond the individual seems to us an aim worthy of much labor."

MENNINGER, Topeka, Kan.

THE TREATMENT OF GENERAL PARESIS BY INOCULATION OF MALARIA. WAGNER-JAUREGG, J. Nerv. & Ment. Dis. **55**:369 (May) 1922.

TREATMENT OF PARESIS BY INOCULATION WITH MALARIA. H. F. DELGADO, J. Nerv. & Ment. Dis. **55**:376 (May) 1922.

Wagner-Jauregg used a strain of malaria parasites obtained from the blood in a case which had not been treated with quinin, thus increasing the susceptibility to the drug when cure was desired. After one general paralytic had been inoculated, succeeding cases were inoculated by the injection of infected blood from the first case. Typical paroxysms of malaria appeared after an incubation period varying between six and thirty-six days. Eight or nine attacks were usually permitted to occur and the malaria was then checked by quinin; recovery occurred in all cases. Complete remission of symptoms of general paralysis occurred in all cases of short duration; remissions also took place in cases of early dementia, severe maniacal excitement with delusions of grandeur, and paralytic attacks. A course of neo-arsphenamin was given after the quinin therapy. No constant change was noted in the Wassermann reaction, globulin content, or cell count of the cerebrospinal fluid.

Delgado used the technic of Wagner-Jauregg, and reports four cases of general paralysis treated by malarial inoculation, as well as a case of probable dementia praecox or cerebral syphilis. This patient was accidentally infected with *plasmodium vivax*, and supplied the blood for the general paralytic cases. In two of the cases complete cure apparently took place; one patient improved greatly; one patient died—this was an advanced case with marked psychomotor agitation and with urinary and fecal incontinence. The author feels that there is ground for optimism in regard to the prognosis in general paralysis and calls attention to the views of Spielmeyer and Weichbrodt concerning the possibility of anatomic cerebral restitution. The author also notes that since ancient times, in one locality in Peru, the people treat leishmaniasis of the skin and mucous membranes by exposing themselves to malarial infection.

There is a tradition that, after a number of malarial attacks, the skin lesions heal. This is of interest because of the zoological relationship between leishmania and the spirochete of syphilis, and because in both infections arsphenamin is efficacious as a curative agent.

VONDERAHE, Philadelphia.

THE ETIOLOGY OF PHOBIAS. ENGLISH BAGBY, J. of Abnor. Psychol. **17**: 16 (April-June) 1922.

The writer presents two cases in which a phobia was removed by the discovery, in both cases accidental, of the etiologic psychic trauma. In the first case, a woman since childhood had been terrified at the sound of running water. This was eventually explained by an experience which occurred at the age of 7, when she seriously disobeyed an aunt; she ran away and became lodged in a wedge in the rocks beneath a water fall. All of this was concealed from her mother. The second case was that of a man who at the age of 55 discovered the cause of an abnormal terror of being grasped from behind. He traced it to an episode which occurred in the village grocery store, where, as a boy, he had been seized suddenly by the groceryman as he was stealing peanuts and had thereupon fallen screaming to the floor.

The writer frankly acknowledges that more thorough explanation could be made from the Freudian standpoint. He concedes that it would "be easy to see how a sex act would, in many cases, supply the element of guilt" but does not feel that in these two cases sex factors were present. He strangely omits to mention his indebtedness to Breuer, whose now little heard theories he tacitly supports or to concede that transference alone often yields rapid but temporary "cures."

MENNINGER, Topeka, Kan.

THE "NUQUO-MYDRIASIS" SIGN. E. FLATAU, Rev. Neurol. **28**:1200 (Dec.) 1921.

Flatau describes a new clinico-diagnostic sign—the mydriasis which follows neck flexion, and persists during the maintenance of this position and often for several seconds longer. This sign is present particularly in epidemic and tuberculous cerebrospinal meningitis in which cervical flexion is attended by pain, and the absence of sluggish pupillary reaction to light. It seems most marked in the acute and pre-agonal phases of such disorders, and in general seems to parallel other signs of meningismus, particularly the Kernig and Brudzinski signs. It has also been determined in serous meningitis following purulent otitis media, in hemorrhagic pacchymeningitis, in third ventricle tumor with ventricular and sub-arachnoid hemorrhages, and in cervical spondylitis; but has not been determined in poliomyelitis with cerebral features, multiple sclerosis, tabes, uncomplicated intracranial neoplasms, epidemic encephalitis, functional disorders and non-neuraxial infections. In this respect it is of distinct value in differential diagnosis. As to the mechanism involved, the author finds this reflex to be: initiated through stimulation of the sensory endings in the field of the cervical vertebrae; transmitted along their fibers to the cervical cord; via the spinothalamic tracts to the ventral part of the thalamus and the hypothalamus; returned via the peduncles to the cervical cord; and distributed via the seventh and eighth cervical and first and second dorsal anterior roots to the superior cervical ganglions, and also over the first division of the trigeminus to the ciliary nerves, and finally to the dilatores pupillae.

RAPHAEL, Ann Arbor, Mich.

CERVICAL NEUROFIBROMA. Edward Flatau and Bronislaw Sawicki, L'Encéphale **17**:617 (Dec.) 1922.

The case reported is that of a woman, aged 63, who for many years had an egg-sized, smooth, elastic and painless tumor in the left anterior triangle of the neck. It increased in size for a period of two years and the growth was accompanied by mild pains in the left side of the neck and down the left arm. There were no other symptoms and examination revealed no evidence of organic disease of the nervous system. At the necropsy it was found that the tumor originated near the posterior ganglion of the third cervical nerve. It extended outward through the intervertebral foramen, which was much enlarged, and ended distally in a cyst. The outer wall of the cyst was composed of nerve fibers; the inner wall was composed of connective tissue and had undergone cystic degeneration. The authors comment on the rarity of this condition and have collected only five similar cases from the literature.

They conclude from a study of their own case and the five previously reported that these tumors are evidenced first by the appearance of a swelling in the neck and, later, by symptoms of cord compression. Operation relieved the symptoms, and there was no instance of recurrence. The authors hold that these tumors originate in the proximal portion of the nerve and extend distally. In some instances they may originate within the spinal canal. The condition is not allied to Recklinghausen's disease; the nearest analog is the cerebellopontine angle tumor.

Hyslop, New York.

TEMPERAMENT IN HARMONIOUS HUMAN RELATIONSHIP. M. J. Ream, J. Abnor. Psychol. **17**:58 (April-June) 1922.

"Rarely has the experimental method been used in attacking problems in human relationship." This work was carried out in a course of instruction at the School of Salesmanship of the Carnegie Institute of Technology. Ream's purpose was to answer the question with which he begins his article, "Do we prefer to work with people having temperaments similar to our own or . . . with contrasting temperaments?" He used a questionary method, and asked which of six given persons would be selected as a companion under certain conditions. These six, as well as the straw voters, had been previously grouped according to the Downey will-profile test as mobile (psychiatrists would understand better the term hypomanic and philosophers might prefer sanguine), or deliberate (phlegmatic). The conclusions rather strikingly indicated that the mobile types were more popular and that they prefer to work with persons of similar temperament, other things being equal. The selectors possessing a deliberate type of temperament were evenly divided in their preferences for companions.

Menninger, Topeka, Kan.

SEPTUM LUCIDUM TUMOR. Souques, Alajouanine and Bertrand, Rev. Neurol. **29**:270 (March) 1922.

In the case reported, seemingly the first to appear in the literature, there was practically no anamnesis available, except an indefinite report of headaches, apparently of long standing. On examination the patient, a woman, aged 44, was found to be much deteriorated mentally in all fields, the reaction being essentially one of pronounced disorientation and confusion. Neurologically, there were noted: pupillary inequality with sluggishness in reaction to light, urinary incontinence, slight rigidity in leg-thigh flexion, slight lingual

tremor with complaint of severe unlocalized headache, and paresthesias of the lower extremities. Laboratory examinations, including examination of the spinal fluid, were quite negative. Examination of the ocular fundi was not carried out. The clinical course was one of rapidly progressing dementia, unattended by further neurologic developments, and death occurred after six months from pneumonia. The necropsy disclosed a glioma about the size of a hen's egg, with cystic and calcareous changes, which had developed primarily in the septum lucidum, and was associated with internal hydrocephalus and pressure effects upon the corpus callosum and cortex.

Comment is made upon the diagnostic difficulty presented by this case from the lack of localizing features; the outstanding reaction was merely a rapidly progressing dementia which, in this case as well as in others implicating the callosal field, the authors feel to be essentially of a secondary nature and dependent upon the associated, greatly increased, intracranial pressure.

RAPHAEL, Ann Arbor, Mich.

THE MENINGEAL SYMPTOMS OF ASCARIASIS. H. TURCAN, Presse méd. **30**:844 (Sept.) 1922.

The writer describes a typical case of ascariasis and calls especial attention to the differential diagnosis between this and tuberculous meningitis. Ascarids frequently cause general nervous phenomena: contractures, paralysis, and signs of meningeal irritation; less often they cause other phenomena. One case which simulated an acute mastoiditis is briefly noted. The pathologic change is still in dispute, but arguments are adduced against the theory of meningismus or pseudomeningitis, with reflexes caused by the direct irritation of nerve terminals in the intestines, and in favor of the theory of an actual toxic meningitis.

HUDDLESON, New York.

PLATO: A FORE-RUNNER OF PSYCHO-ANALYSIS. OTTO PFISTER, Internat. J. of Psychoanal. **3**:169 (June) 1922.

Pfister, a minister of Zurich, has made an effort to apply psychanalysis in his professional work, and is a member of the International Association. This article attempts to point out that Plato held views which coincide with the theory of psychanalysis (a thesis which was presented as early as 1915 by Nachmansohn). Pfister emphasizes Plato's eulogy of love, particularly physical love (which includes even homosexual love), and his unification of the love of God, the love of spouse, the love of child, and the love of mankind. Plato's conceptions of conflict are also considered parallel by Pfister and a few quotations will illustrate the points he emphasizes: "There are in the human body these two kinds of love; the desire of the healthy is one and the desire of the diseased is another. . . ." "The best physician is he who is able to separate fair love from foul, or to convert one into the other; and he who knows how to eradicate and how to implant love, whichever is required, and can reconcile the most hostile elements in the constitution and make them loving friends, is a skilful practitioner. . . ."

MENNINGER, Topeka, Kan.

THE STUDY OF VESTIBULAR NERVE FUNCTION IN MYXEDEMA. ROY A. BARLOW, Am. J. M. Sc. **164**:401 (Sept.) 1922.

Barlow notes from the work of previous observers that deafness is a frequent symptom in myxedema and also in cretinism. Fifteen cases of myxedema

were studied. Bárány tests revealed a retardation in response in 73 per cent. of the cases. Seven showed spontaneous nystagmus. In three cases there was lowered bone conduction. No spontaneous pointing fault was noted. The tests were accompanied by basal metabolic determination, but the changes in the ear function bore no apparent relationship to the metabolic rate. The clinical vestibular picture in myxedema, in the author's opinion, is definite and referable to delayed response to stimuli.

VONDERAHE, Philadelphia.

FAMILIAL INFANTILE BULBAR PALSY. E. D. PAULIAN, Rev. Neurol. **29**:275 (March) 1922.

Attention is directed to the apparent rarity of this condition. Only three authentic cases have been described thus far in the literature, the protocols of which the author discusses in full. On this basis, and his own experience, this disorder seems to have its onset most usually between the ages of 5 and 20. Paralysis (bilateral) of the superior division of the seventh cranial nerve appears to be the clinical feature which first becomes manifest, and is somewhat exceptionally accompanied by involvement of the middle and inferior divisions. As the syndrome develops, the tongue becomes atrophied and shows fibrillary tremor, and there are associated paresis of the pterygoid, masseter and palatine muscles, with corresponding disturbance in phonation, mastication and deglutition. Vagus and accessory paresis next present themselves and there are consequent respiratory difficulty and atrophic changes in the cervical musculature. The reflex field, however, is reported as essentially unchanged and there seems to be no indication of pyramidal disturbance. Death occurs after a relatively chronic course, either through inanition or aspiration pneumonia, or as a result of acute bulbar failure. Paulian comments upon the obscurity which obtains as to the essential etiology and pathology of this disorder. In connection with the latter, he mentions the possibilities of basic mitochondrial disturbance, ascending polioencephalitis and essential neuraxial agenesis, specifically of the cranial nerves.

RAPHAEL, Ann Arbor, Mich.

AORTITIS AND TRIGEMINAL NEURALGIA. J. MINET and R. LEGRAND, Presse méd. **30**:773 (Sept.) 1922.

Five cases are presented, which showed the "aortitis-trigeminal neuralgia syndrome." Central cerebral arteritis is thought to account for the neuralgia rather than sclerosis of the vasa nervorum. In one case, resection of the cervical sympathetic and of the first thoracic ganglion brought about an improvement in the aortitis. In other cases, improvement was obtained (at least of the neuralgia) by vasodilator and hypotensive medications or else by antisyphilitic treatment.

HUDDLESON, New York.

Society Transactions

BOSTON SOCIETY OF PSYCHIATRY AND NEUROLOGY

Annual Meeting, Jan. 18, 1923

F. H. PACKARD, M.D., *President, in the Chair*

AN UNUSUAL CASE OF BRAIN TUMOR. DR. G. A. WATERMANN.

The patient, a man of 40, had been suffering from attacks of aphasia for fourteen years. The first year there were several epileptiform convulsions. During subsequent years there were attacks of aphasia, sometimes with nausea and sometimes with amnesia. He might go several days without these attacks; often they would occur many times during one day. There had been no headache, vomiting nor optic neuritis at any time in the course of the disease. The patient had suffered from attacks of ophthalmic migraine and also of asthma during his life in college; they had persisted every year since. When first seen by me he had been having jacksonian seizures for seven or eight years. These consisted of numbness that involved first the right foot, then extended up the body to the right cheek and ear, and finally down the right arm into the fingers; the numbness then passed off, the whole duration being one-half to one minute. These seizures followed the migraine attacks, with which were associated right-sided scotoma and right hemianopia.

In 1921 and 1922 the patient had a series of misfortunes: his father died, his mother had pneumonia, his boy had an accident that proved almost fatal, and much extra business responsibility was thrown upon him. Early in 1922, he began to have more and more lassitude, and the aphasia became almost constant, so that through the summer he found it difficult to converse and very difficult to understand what was said. The attacks of dizziness increased to twenty or thirty a day. He was unable to read although he still could play the piano and read music at sight. He found it difficult to understand simple questions and directions, and could scarcely speak a sentence without using wrong words or stopping to think of a word which he could not remember. In trying to read he would get two or three words very slowly and then be unable to go further.

The physical examination in October showed practically a normal condition. The pupils, optic nerves and retinas were normal; there was no nystagmus, and no change in the fields of vision, nor eye movements. Hearing was normal. The tongue was protruded straight without tremor. Grasp was normal in both hands. The wrist reflexes were absent. There was no ataxia, asynergy, adiadokokinesis, nor astereognosis. The knee-jerks were moderately active, and there was neither ankle clonus nor Babinski sign. The heart was normal with systolic blood pressure 120. The Romberg test was negative and he could stand comfortably on one foot indefinitely.

Through October and November the symptoms were sometimes better and sometimes worse. December 18, he suddenly became unconscious for a few minutes at the table. He was put to bed and throughout that day had increasing headache with almost constant vertigo, and seemed very sick. In the evening he vomited, fell into a deep sleep, and died shortly after midnight.

Postmortem examination revealed an extremely soft tumor, pinkish in color, that involved the whole temporal lobe from the tip to the posterior part below the angular gyrus. It occupied about one third of the substance of the lobe.

The interesting feature of this case is that the attacks of aphasia dated back for fourteen years, although persistent aphasia had existed only about six months. Microscopic examination revealed the fact that the tumor was undoubtedly of recent development, and that the earlier aphasic attacks and convulsions had been due to a degenerative process in the temporal lobe. The tumor was made up of rapidly growing cells as indicated by the presence here and there of mitotic figures; it was very vascular and contained many small hemorrhages. Scattered through the tumor were numerous masses of calcified corpora amylacea; but these bodies existed also in the uninvolved brain tissue and thus indicated a previous degenerative change in the temporal lobe which had subsequently been invaded by the tumor. It seems probable, therefore, that the earlier attacks of aphasia were due to a degenerative lesion of the temporal lobe, and that the latter, intensified symptoms were due to a glioma in this region, that perhaps developed in some indirect manner as the result of the intense mental strain to which the patient had been subjected.

DISCUSSION

Dr. G. L. Walton: The duration of efficiency in spite of the gradual growth of a tumor of this variety gives the case a special interest. There can be no question that the tumor was the cause of the symptoms present when I saw him in 1909, though I have no recollection of the process of reasoning by which I reached the diagnosis. Indeed, until reminded of it by Dr. Waterman (and by Dr. Clap, to whom I sent him for ocular examination) I did not remember that I had done so. My notes, however, would indicate that epilepsy was made improbable by the prominence of gastric symptoms, hemianopia, and aphasia at the time of the attacks, as well as by the persistence of aphasia after consciousness was recovered; that migraine was excluded by the loss of consciousness and lapses of memory, as well as by the aphasia; this last would have been only fleeting and premonitory, in the usual event that it were a symptom of this disorder. As in this case, the question whether long standing migrainous attacks were connected with the new growth or merely coincidental, came up in the case of Dr. D. that many of us remember; he died from pituitary tumor at the age of 28, but had been subject to attacks of migraine, preceded by hemianopia, for a great many years. In that case, however, the hemianopia became permanent during the last year of his life, which seemed to show that the "sick headaches" were other than a coincidence.

Dr. W. J. Mixter: I feel that this case has a real lesson, namely, that when new growth is suspected, operation is indicated even in the absence of choked disk or other evidence of general pressure. Focal epilepsy is frequently an indication of a local process involving the cortex, and as such requires exploration. We are all of us too prone to await the onset of general pressure symptoms before advising operation. The neurologist should remember that the difficulties and dangers of exploratory craniotomy are remarkably increased by increased intracranial pressure.

I am perhaps a radical, but I am strongly of the opinion that cases of focal epilepsy should always be explored. Operation in Dr. Waterman's case could have been palliative only, but to my mind would have been indicated, especially as I thought from the history that the lesion was probably an

arachnoid fibroma or a localized collection of fluid beneath the arachnoid rather than a glioma. An osteoplastic craniotomy, such as would be performed in a case of this kind, should expose the motor cortex from the lower edge of the leg area down, and also most of the temporal and part of the frontal lobes.

BARBITAL INTOXICATION. Dr. A. Warren Stearns.

During the past five years certain cases have come to my attention, a unique feature of which is that a single large dose of barbital has caused a state of intoxication, either pleasurable or a relief from unpleasant symptoms, that lasted from twenty-four hours to several days. The evidence does not warrant an opinion as to whether or not this is a peculiar reaction of certain people to barbital.

Case 1.—A man in the sixties, who had been a periodical drinker for many years and had used barbital extensively during the sobering-up period, was found one day in a state of profound intoxication. Movements of the hands were clumsy, the speech was thick, the eyelids heavy, and the reflexes essentially negative. He was mentally clear but thought processes, though accurate, were very slow. He was also somewhat jocose. This state lasted for two days. The patient was seen in several subsequent attacks. In at least one, there was assurance that the intoxication was due to some substance taken before the attack, the effect of which lasted for at least twenty-four hours. It was later learned that this man had taken large doses of barbital; the exact amount was not determined.

Case 2.—A trained nurse in the thirties, who had necrosis in the jaw with a great deal of neuralgic pain and insomnia, was found one day in a state of intoxication which at that time was believed to be alcoholic. Subsequent investigation satisfactorily ruled out alcohol. I first saw her in the evening; she had returned home late in the afternoon in an intoxicated condition: very unsteady, speech thick, eyelids heavy. The reflexes were unaltered. It was supposed that she had taken some drug, so her clothes were taken away and she was closely observed. She slept a little but for the most part remained in this condition for two days. I saw her in several subsequent attacks without knowing the cause of the condition until finally her brother saw her take the whole contents of a tube of barbital tablets containing 100 grains. The intoxication from this dose lasted about forty-eight hours.

Case 3.—A man in the forties, a chronic alcohol addict, was found in a condition very similar to the above but with no alcoholic odor on his breath. He admitted that for the past year he had been taking barbital in doses of from 60 to 75 grains, that produced an intoxication lasting from twenty-four to forty-eight hours.

Case 4.—A man in the late forties, who had had repeated operations for gastric ulcer and had complained of great pain, was found unconscious one day and was supposed to have attempted suicide. After twenty-four hours he woke comparatively clear. He has since been observed in several attacks like those already described, and has admitted taking from 20 to 40 grains of barbital for the purpose of producing this state.

Case 5.—A man in the forties complaining of gastric distress and insomnia, had taken barbital in an attempt to get relief. While on the train with his brother, he took the contents of a tube of barbital tablets; the exact number is not known. When seen six hours later, he was clumsy, unsteady, and the

eyelids drooped so as to obscure vision; the knee-jerks were absent. The next morning when I saw him he was in the same condition except that the reflexes were all active. The following morning he still showed symptoms, but they were less marked. He admitted taking large doses of barbital in order to get relief from his symptoms.

DISCUSSION

DR. F. J. FARNELL: In several cases of barbital as well as phenobarbital poisoning seen by me during the last few years, all have presented absent superficial reflexes.

DR. F. H. PACKARD: While I have no definite memory of the details of the cases, I remember that many years ago Dr. Tuttle told me of the possibility of poisoning by barbital; he had seen a number of cases. In those cases, as I remember it, barbital was not taken for the purposes reported by Dr. Stearns; the poisoning was accidental. Barbital was a comparatively new drug at the time and as veronal was advertised as harmless, in contrast to some other hypnotics, poisoning resulted from taking large doses when small doses had not produced the desired results. Poisoning by bromid, which Dr. Walton has mentioned, used to be rather commonly seen at the McLean Hospital; many patients arrived in a state of delirium, much exhausted physically, with badly coated tongue and sordes on the teeth. There were frequently paraphasia and aphasia, and a bromid eruption was usually to be noticed. These were very gratifying cases to care for, as with withdrawal of drugs, proper catharsis and feeding, they very speedily recovered. The usual history was that because of nervousness and sleeplessness the family physician had begun by giving small doses of bromid, which had been increased to large doses in an attempt to produce the desired effect, and had been continued regularly for some time. As a rule the history indicated that little food had been taken for some days. I have seen many such cases outside in consultation, where a removal of the bromid and feeding soon resulted in the patient's recovery.

THE PSYCHIATRIC IMPORTANCE OF THE KUHLMANN TESTS.

DR. JAMES S. PLANT.

A new age-level set of psychologic tests, which were standardized largely upon institutional cases, is presented. The present study deals with results in the unselected and varied material that comes to the Judge Baker Foundation. These tests stress mental control. They have the following advantages over the Terman tests: (1) being new there is less likelihood of previous coaching; (2) the responses are far less open to interpretation; (3) they are largely performance tests; and (4) they involve language to a much smaller extent. They have the following disadvantages: (1) they require a little longer time and demand much more sustained attention, and (2) they are very hard to motivate.

Forty-five unselected cases have been used. Eight of these were mildly psychotic or "pre-psychotic." Psychiatric diagnoses were made by other physicians without knowledge of the test results. All cases were also given a wide range of other tests.

Normal cases showed a correlation between Kuhlmann and Terman tests of 0.95 with a probable error of $\pm.01$. With one exception the "psychotic" cases showed much lower Kuhlmann than Terman intelligence quotients. The least difference between the Terman and the Kuhlmann intelligence quotients

for psychotic cases was as large as the largest difference for any normal case. In one psychotic case the Kuhlmann intelligence quotient was 26 points lower than the corresponding Terman.

"Mental control" is largely dependent upon the affective life. Psychologic tests have almost entirely busied themselves with intellectual functions. It is a matter of great psychiatric importance that a set of *standardized* tests have touched, however roughly, the emotional field.

F. L. WELLES, PH.D.: It is not clear to me just how Dr. Plant regards mental control and emotion, but it seems that he looks upon them as very close together, in that great fluctuations of a test dependent on mental control indicate instability of emotional life. The balance of probability is on this side, but it is doubtful if the Kuhlmann tests differ in this respect from a considerable number of standardized performance tests, such as those worked out by Pintner and Patterson. In this respect the Kuhlmann tests do what is done by any test involving continuous effort, of which there are many. Lesser correlation in psychotic, as compared with normal, material probably exists between any two tests. The Stanford scale correlates with itself, so to speak, least in psychotic material. It has been found most regular with normals, less so with feebleminded, still less with psychotics in general, and least regular of all in organic or toxic conditions. In general, new scales nowadays add little in the way of more accurate methods of measuring intelligence, though some, like the Myers Mental Measure, make advances in convenience and practical serviceability. New test series are advantageous to have, however, as alternates to old tests with which the patient has become familiar. The Kuhlmann tests are a welcome addition to psychometric resources, but special distinction claimed for them is perhaps open to question.

CHICAGO NEUROLOGICAL SOCIETY

Regular Meeting, Jan. 19, 1923

H. I. DAVIS, M.D., *President, in the Chair*

PARALYSIS AGITANS IN A GIRL OF TWELVE. DR. W. G. STEARNS.

In this case the typical tremor of Parkinson's disease is present in the hands, arms and shoulders of both sides. The patient feeds herself with great difficulty. She can write legibly but only by pinning the forearm of the right hand beneath the weight of the body. The upper extremities lack markedly in muscular power when compared with other muscles of the body. There is only a slight amount of rigidity in the affected muscles, but the characteristic, slightly semiflexed condition is present. The muscles of the head and neck are not affected. The muscles of the trunk, except those about the shoulders and those of the lower extremities, remain unaffected. There is no tremor during sleep. There are no disturbances of sensation and the reflexes are normal.

In early childhood this patient had chickenpox, mumps and measles. At 6 years of age she "fell down the cellar door," but was apparently uninjured. She was an active robust child. At the age of 12 the tremor first appeared, equally in the two hands; it has very gradually increased in amplitude and has slowly extended to involve the hands, arms and shoulders. At 13, men-

struation was established normally. At 14, she had her first sore throat. At the present time the patient is 16 years of age and is, except for the condition of the arms, in good health, strength and spirits. She is in the third year at high school and appears normal mentally.

CYCLOPLEGIA IN A GIRL OF TWELVE. Dr. W. G. Stearns.

This patient, a girl aged 10, complained that near vision was blurred, and was unable to read even the very largest newspaper headlines. She was hypersensitive, irritable, and unable to concentrate her attention. In early childhood she had measles, whooping cough and chickenpox, all in mild form, and has never had any serious illness.

Nov. 16, 1922, she had fever at night, and her throat was sore with gray spots on it. Her mother treated the throat with tincture of iodin and a mouth wash. She promptly recovered and was out of school for only one week. December 3, seventeen days later, she could not read. December 19, about five weeks after the onset, they first consulted an oculist, who found complete paralysis of accommodation. She had 2.25 diopters refraction error and was given a corresponding lens; this enabled her to read at 16 inches, but no less. The pupils were not dilated, and reacted well to light; the eyes were otherwise normal. Weekly visits were made thereafter, and December 26, forty days later, the oculist's findings were the same. She was then referred for an opinion as to the pathogenesis. She had at that time a slight nasal twang to her voice, which suggested paresis of the soft palate. January 2, the condition was much the same but the nasal quality of tone had disappeared. January 16, the pupils were normal, reacted promptly to accommodation as well as to light, and vision was normal.

There can be no doubt that on November 16 the child had diphtheria. Two and a half weeks after the diphtheria, disturbance of vision appeared. At the first examination, the oculist found complete loss of accommodation with normal reaction to light. My excuse for presenting this case is that there was such clear-cut, well defined and complete loss of accommodation, in spite of which the pupils behaved normally in every other way.

DISCUSSION

Dr. Sanger Brown: What was the condition of the deep reflexes when the cycloplegia was at its height?

Dr. Peter Bassoe: I would like to ask if there is any possibility that the first patient had a mild attack of epidemic encephalitis. We do see paralysis agitans-like syndromes following encephalitis of the ambulatory type. I saw such a case in the dispensary last week in a young man who gave a history of having had a mild indisposition in October, 1919. He saw double for a couple of days and stayed away from work one day only, but I believe, in view of his present condition, that this was enough to justify a diagnosis of encephalitis. True paralysis agitans in a child of 12 is extremely unusual.

Dr. Hugh T. Patrick: Did you consider the possibility of Wilson's disease or pseudosclerosis in the first case?

Dr. W. G. Stearns: In the second case the deep reflexes, including the knee-jerks, were slightly increased. The patient was easily irritated and hypersensitive.

In the first case I could get no history of any untoward events in the child's life except her falling "down the cellar door" when between 6 and 7 years of age. She had not menstruated at the time of this trouble and had never had a sore throat until she was 14. I had not considered Wilson's disease.

A CASE OF CONCUSSION OF THE SPINAL CORD WITH A CLINICAL PICTURE OF AMYOTROPHIC LATERAL SCLEROSIS. Dr. G. B. Hassin.

This article will appear in full in a later issue.

HYSTERICAL AMNESIA FOLLOWING PHYSICAL INJURY—A CASE STUDY. Dr. Charles F. Read.

The patient, a man, aged 26, with a somewhat neurotic background, suffered a slight injury while working in a coal mine, Oct. 11, 1922. He was struck over the right shoulder blade by a falling piece of coal a little larger than two fists; he did not become unconscious but complained of being dizzy and soon began to act queerly. He was taken to a hospital where he exhibited some hysterical behavior; following this he came to himself with an amnesia which extended back to Jan. 7, 1914.

Inquiry revealed the fact that prior to the latter date he had become involved in an affair at school with a married woman, and, after a quarrel with a friend who ventured to advise him in the matter, the patient "lost himself" for a period of several days; following this he "came to" in a mining town hospital in October, 1922. Aside from some vague dream-like recollections, entirely disoriented as to time and place, the amnesia was complete when the writer saw him some weeks after the accident. Simple inquiry failed to accomplish anything by way of free association so, inasmuch as the time was short, the patient was hypnotized and the memories of the intervening years were readily recovered. A day or two later in the waking state the patient succeeded in recovering these memories and was soon able to leave the hospital.

The case is of interest, because, although the amnesia followed physical injury, it was entirely of a hysterical character and was very probably occasioned by the fact that the patient, naturally of an artistic sensitive makeup, and with a history of a previous flight when a youngster, had gone to work in the mines because of a sense of duty toward a tuberculous sister. Two uncles had been killed in the mines and two brothers injured; the thought of the mines disgusted him, but in spite of this, in order to help the sister, he mined coal during the day, while for his own pleasure he wrote upon a novel at night. The conflict between a sense of duty and the desire for artistic creation gave rise to the final dissociation, which was precipitated by the slight accident in the mine.

Recovery was symptomatic and should be followed by psychanalysis until the patient becomes acquainted with his own personal makeup and learns how to deal with it; else there will very possibly be other hysterical flights of one kind or another in the future.

DISCUSSION

Dr. Clarence E. Neymann: I would like to ask Dr. Read if he had an opportunity to go into this patient's period of conflict at the age of 17. It seems to me that in his amnesia he gets out of one conflict, coal, dust and grime, and throws himself headlong into a sexual conflict. Did he find any

enjoyment in the comparison between the fairy-like creature and the barbaric beauty? Is there not behind that some lack of sexual satisfaction in the intervening years, and is he not the sort of person who always wants a sort of pot-pourri, the heavenly and earthly love? If he is that sort of person, is this not the cause of the amnesia, rather than the fight with the dirt and grime of poverty? Would that not explain why he included the army period, because in this army work he had no chance to enjoy the heavenly and earthly love which he evidently desired?

DR. RALPH C. HAMILL: I have been working on a case of amnesia for some time in a young man who stole, on two different occasions, and then went into periods of amnesia; the first one lasted from the time he got out of the army until his stealing was discovered, which covered a period of, as I recall it, a little over a year. With him, as with this patient of Dr. Read's, it was very interesting to note the emphasis which he put on his fear of his father's finding out about it and the punishment that would be meted out to him by his father. Then it was interesting that the first person from whom he stole reminded him very strongly of his father. Unfortunately, he got away from me before I managed to connect up, as satisfactorily as I think could have been done, the relation between stealing from this man who resembled his father and early, youthful experiences; but there was the very strong feeling of fear in his mind, especially of punishment being meted out to him by his father.

DR. CHARLES F. READ: I do not know just what to say in response to Dr. Neymann's question. The patient evidently did get some considerable enjoyment in writing out the story of his attachment to these two women; it is, perhaps, not unusual in the male sex, to take pride in their amours. Just what relationship this bears to his amnesia is problematic. I did not get back at all into his very early life and therefore do not know what his personal makeup is, as I acknowledged. I merely secured a symptomatic recovery. Evidently he had learned how to become amnesic and, when the second crisis came, snapped back through the intervening years, through his period of artificial war-time sublimation, back into the days preceding the first amnesia.

PHILADELPHIA NEUROLOGICAL SOCIETY

Regular Meeting, Jan. 26, 1923

CHARLES H. FRAZIER, M.D., *President, in the Chair*

TELANGIECTASIS OF THE SPINAL CORD. DRS. WILLIAM G. SPILLER, and CHARLES H. FRAZIER.

This report will be published in full in a later issue of the ARCHIVES.

A MENINGIOMA BOTH INTRADURAL AND EXTRADURAL, REMOVED FROM THE SPINAL CORD WITH COMPLETE RECOVERY. DR. WILLIAM G. SPILLER.

History.—The patient, a woman 20 years of age, began to be weak in the lower limbs in April, 1922, having been entirely well until this time. She fell several times during April and on one occasion slipped to the bottom of

the stairs but was not injured. She had occasionally during May some stiffness and numbness in the lower limbs, but these were not persistent. Her gait was a little incoordinate. The little finger of each hand began to be numb. On July 19, the right patellar reflex was about normal and the left a little exaggerated. The right Achilles reflex was not obtained and the left was about normal. The Babinski reflex was not typical, for while the slightest irritation of the sole of either foot caused the big toe to assume a position of persistent overextension, the position may have been the result of voluntary movement. She was able to walk with very little incoordination. She had no distinct impairment of objective sensation.

The patient had had much mental disturbance, family affairs had excited her, and as she undoubtedly improved under psychotherapy, it was impossible to exclude at that time a psychic complication. It seemed best to have her go away to the seashore for a short time with the understanding that if she should get worse she would return for observation. It would have been unwise to recommend operation until the symptoms became more pronounced and the patient would not have accepted operation at that time. She did not return from the shore until late in the summer, and did not agree to have an operation until October. Her condition then was much worse and was as follows:

Heat, cold and pain sensations were impaired in the lower limbs and trunk as high as the second intercostal space on each side, and on the inner side of each upper limb as far as the hand. Tactile and vibration sensations were not impaired. The patient stood with the greatest difficulty, even when supported, but if supported she could take a few steps with the right heel fully 2 to 3 inches from the ground and this heel could not be brought to the ground, whereas the left heel could be placed on the ground. The right leg could not be fully extended on the thigh on account of contracture of the flexors of the legs. The spasticity of the lower limbs was excessive and interfered with obtaining the tendon reflexes, but occasionally when it was less the patellar reflexes could be obtained and were exaggerated. The feet were in extension and spasticity prevented ankle clonus. A very typical Babinski reflex was present on each side.

The little and ring finger of each side were partially flexed at the phalangeal articulations, especially the little finger, and the muscles of each hand were somewhat atrophied. The biceps and triceps reflexes were lost or nearly lost on each side. There was no ocular sympathetic paralysis.

The signs all pointed to a lesion having its upper level about the eighth cervical segment, and affecting the lateral and anterolateral portion of each side of the spinal cord. The posterior columns and posterior roots evidently had escaped, for there had not been any pain at any time except the discomfort caused by the spasticity. The right side of the cord seemed to be a little more affected.

The diagnosis made before the operation was tumor on the anterior part of the spinal cord at the eighth cervical segment.

Operation.—Nov. 1, 1922, the laminae of the fifth, sixth and seventh cervical and the first thoracic vertebrae were removed. On a line beneath the lamina of the sixth cervical, there appeared on the right side of the cord what was thought at first to be an extradural tumor. In rongeuring away the lamina toward the right, it was found that this tumor extended a distance of 1 or 2 cm. into a bony cavity about 2.5 cm. long, 2.5 cm. deep and 4 cm. across from

the lamina on the left side to the bony wall of the cavity on the right. In attempting to liberate the tumor from the dura it appeared to be firmly attached at one point and on closer inspection was found to continue within the dural sac. A T-shaped incision was then made in the dura and a small intradural tumor lying on the anterolateral aspect of the cord was found. It was free from all attachments and readily enucleated. The larger growth, however, was very firmly attached at its base, which appeared to be at the outer side of the bony cavity, so that in its removal portion of the capsule was stripped from the tumor. It is difficult to determine where the tumor originated. The intradural tumor had made but little impression on the cord and the larger extradural tumor, because of the size of the cavity in which it lay to the right, caused little pressure on the cord. None of the roots passed over the extradural portion of the tumor.

For several days after the operation the spasticity and involuntary jerking of the lower limbs were excessive and caused the patient great pain, but this gradually ceased. The lower limbs regained their normal power, the impairment of heat, cold and pain sensations in the lower limbs disappeared and the patient now has little or no symptom caused by the tumor.

Pathology.—Examination of the tumor showed it to be an endothelioma, or possibly a fibroma. It is sometimes difficult to distinguish between these two forms of tumor occurring in the central nervous system as sections from one part may resemble a fibroma and from another part of the same tumor may have the appearance of endothelioma. Perhaps one may best solve the difficulty by employing the noncommittal name of meningioma suggested by Cushing.

It would seem that the tumor had its origin probably from the place of exit of the spinal roots from the vertebral canal, and that it gradually wore away the surrounding bone as it grew, making in this way a nest for itself, and thereby causing no pressure upon the spinal cord. The symptoms were evidently caused by the intradural tumor, which exerted pressure on the anterior and lateral parts of the spinal cord. It is exceptional that a tumor should be partly intradural and partly extradural.

DISCUSSION

DR. CHARLES H. FRAZIER: The intradural tumor was elongated and of the size of the average extramedullary intradural endothelioma. Through a small opening the intradural tumor communicated with what I believed to be the primary extradural growth.

AN ENCHONDROMA OF THE BRAIN REMOVED WITH RECOVERY.

DR. WILLIAM G. SPILLER.

History.—D. D., 45 years of age, was admitted to the hospital, May 16, 1922. On Sept. 14, 1918, he was on a train to which was attached a car containing soldiers who had been injured, and he was much affected by what he saw. After awakening on September 16, and while still in bed, he had a convulsion in the right lower limb. It is uncertain whether his right upper limb was implicated, and after the convulsion he was numb on the right side of his body. A physician who saw him while he was in the convulsion diagnosed the condition as hysteria. He had a similar attack in the right lower limb about a month later. The attacks occurred at long intervals until about January, 1921, when they came about once a week. February 3, he had two severe attacks

within one hour, and since then he has been lame in the right foot. His ankle and knee on the right side were affected and his gait became abnormal. In April of this year he had an attack which implicated the right upper limb as well as the right lower limb, and for a time after this attack his right upper limb was powerless, but although he regained much use of this limb he had not been able to write well with the right hand. During the six weeks preceding his admission to the hospital he made many mistakes in calculations, which was striking as he was a bond salesman. He had some difficulty in remembering names and, in reading, he was obliged to read some sentences more than once in order to get the meaning. He had had occipital headache about once a month for years.

Dr. de Schweinitz found the eyegrounds normal. The innervation of the right side of the face in the lower part was a little impaired. Sense of position was impaired in the right hand and this hand showed adiadokokinesis. The biceps and triceps tendon reflexes were a little prompter on the right side, but there was no decided weakness of the upper limb. The right patellar reflex was a little exaggerated. Ankle clonus was pronounced on the right side only, and the Babinski sign was positive only on the right side. The sense of position was distinctly impaired in the right big toe. The right foot turned in and the man walked on the outer border of this foot, and dragged his right toes.

He seemed to have beginning word deafness and word blindness, but these disturbances were slight. His inability at times to get the word he wanted, although he understood all said to him, with some difficulty in reading, were suggestive of early word deafness and word blindness.

The diagnosis was made of a lesion, probably tumor, that irritated especially the center for the right lower limb, but also the center for the upper limb, and implicated the parietal lobe, thus causing, possibly by pressure, slight disturbance of the left angular gyrus and left first temporal convolution. The tumor was believed to be in the motor and parietal region, and as convulsive movement of the lower limb was for a long time the only sign, the tumor was believed to be cortical or near the cortex, especially near the paracentral lobule. Laboratory tests of blood and spinal fluid for syphilis were negative.

A roentgenogram, taken by Dr. Pancoast, showed very distinctly a tumor in the suspected region. The patient was referred to Dr. Frazier for operation, which was performed June 3, 1921.

Operation.—A flap was reflected to uncover the motor area of the left hemisphere. It was noted that the bone was unusually thick at all points and particularly so in the temporal region. On reflection of the flap the tumor at once presented itself in the upper third of the opening. It was hard, fixed, irregular, and adherent to the falx, but was sharply defined and easily separated from the surrounding hemisphere although at several points, venous channels bridging across from the hemisphere to the tumor, had to be tied and cut. The point of origin of the growth, or at least the point of greatest attachment, was an area from 2 to 3 cm. long and 1 cm. wide along the falx at the level of the longitudinal sinus.

In separating the tumor at this point there was sharp bleeding which was readily controlled by tampons. At the conclusion of the operation every attempt to remove these tampons was followed by recurrent bleeding. A fascial transplant at once controlled this. At the conclusion of the operation there was no bleeding from the site of the tumor, but there was from the space between the

dura and the bone. This was controlled eventually by suturing the dura to the galea, thus securing compression of the dura against the overlying bone.

While the wound was being closed the patient was given 600 c.c. of blood from a suitable donor with 500 c.c. of salt solution. The transfusion was divided into two stages, the first portion being given when the wound was about to be closed and the second toward the end of the operation. The wound was closed without drainage.

The pathologic diagnosis was enchondroma.

The patient made a satisfactory recovery and was seen in September, 1922. At that time his condition was about normal except that he was still a little lame in the right foot.

PRESENTATION OF A CASE IN WHICH A PRESUMPTIVE DIAGNOSIS OF TUMOR HAD BEEN MADE THREE YEARS BEFORE.

DR. CHARLES H. FRAZIER.

This case is presented because of the entire freedom from symptoms of intracranial pressure after a period of over three years. A diagnosis presumptive of tumor was made and decompression performed Nov. 28, 1919.

M. F., aged 25, was referred to the neurosurgical service of the University Hospital by Drs. William G. Spiller and Charles Schoff. She has three brothers, all of whom are regarded as "backward," but the patient is quite normal, having graduated from high school and college. In November, 1918, she had a severe attack of influenza after which she had headache that gradually became worse, until in May, 1920, she was admitted for observation to the hospital. The family said they were afraid she might hurt herself as she wanted to press her head and even butt it against the wall. At times her physician said she was quite "flighty" and she suffered from insomnia. She complained of ringing in the right ear, inability to open the right eye as well as the left, and dizzy spells.

On admission to the University Hospital she was examined by Drs. Spiller and de Schweinitz. The positive findings were very few: the lower part of her face was a little coarse suggesting early acromegaly; the tongue was protruded slightly to the right but there were no other cranial nerve palsies. The patellar reflexes were increased, but there was no Romberg sign nor disturbance of gait, and no incoordination. There was a double choked disk of from 4 to 5 diopters with fresh hemorrhages in the right eye; vision in the left eye was two-fifths. Concentric contraction of visual fields was found. The findings suggested intracranial pressure, possibly due to sinus infection.

The subsequent course of events excludes the possibility of tumor, but at the operating table I realized that the symptoms were not due to a neoplasm. When there is a large collection of fluid in the subdural or subarachnoid space, the free escape of which at the operation relieves the pressure at once, one is quite justified in assuming that the pressure phenomena are not of tumor origin. In the absence of a tumor we must assume a lesion of inflammatory or infectious nature, determining a serous meningitis. That this may follow influenza is quite conceivable and my corrected diagnosis in this case is serous meningitis.

The advantages of subtemporal decompression in the presence of a high grade papilledema of doubtful origin could not be illustrated more strikingly than in this case. Dr. de Schweinitz observed that he had never seen a more rapid subsidence of a choked disk. Much has been said of late to discredit the decompressive operation, but it still has a field in properly selected cases and it is in doubtful cases awaiting final diagnosis that the operation should prove of greatest service.

THE ADMINISTRATION OF HYPERTONIC SALT SOLUTIONS FOR THE RELIEF OF INTRACRANIAL PRESSURE. Dr. Temple Fay.

The management of intracranial pressure following trauma or obstruction of the ventricular system by new growths, has offered grave difficulties to the neurosurgeon. The recent work by Weed and McKibbon with hypertonic salt solutions has demonstrated that the intracranial pressure may be rapidly reduced by dehydration, the fluid of the ventricles being reabsorbed into the blood to maintain an isotonic solution.

If 50 to 100 c.c. of 15 per cent. sodium chlorid solution is injected into the veins of a patient suffering from increased intracranial pressure, there will be a decided relief of symptoms within twenty minutes. There will also be a decided reduction of tension and volume of the brain substance. This has been clearly shown in cases where the brain was exposed for exploration and the dura was found to be too tense to warrant opening. Seventeen per cent. of the craniotomies performed by the neurosurgical service at the University Hospital received this salt solution by vein, in order to assist in safely opening and closing the dura in cases with a great amount of pressure. In all but one case it reduced the pressure so that exploration was possible in ten to twenty minutes.

The administration of salt solutions by mouth is somewhat slower and yet quite as effectual. Sodium chlorid is often difficult to take and the patient does not retain it well. Thirty c.c. of a 30 per cent. solution may be used. Cushing and Foley found the brain volume reduced 50 c.c. in one case of dilated ventricles.

The use of magnesium sulphate solution by mouth or rectum has been found in this clinic to be of the greatest value, and very rapidly effectual in all cases of increased intracranial tension. As a preoperative measure it is used as a routine to relieve tension and facilitate exploration. Post-operatively in cases of so-called "medullary edema" where the pulse and the respiration begin to fall rapidly, an ounce and a half of magnesium sulphate crystals by mouth in a glass of water, or 3 ounces of crystals in 6 ounces of water by rectum, will cause a return of the respiration and pulse to normal and relieve the depressed state of the lower centers.

The use of magnesium sulphate in treating all forms of increased intracranial pressure has been very gratifying in our experience of over two years. It will relieve the headache, vomiting and choked disk of the early stages of increased pressure and a patient can be made comfortable until operative intervention can be obtained. It assists in the localization of tumors by removing the pressure symptoms that may mask or exaggerate those of localizing value. In cases of coma and medullary depression when increased intracranial tension was the cause we have seen it bring marked relief. In accident cases with intracranial injury or fracture of the skull followed by the picture of "medullary edema" it is of great value in checking the fall in pulse and respiration, and should be given as a routine, preferably by rectum.

The advantage of magnesium sulphate over saline solution is apparent. It is not absorbed into the blood, as is the sodium chlorid solution, but exerts its action as a hydrogog, rapidly withdrawing fluid from the blood stream into the intestinal tract. This causes concentration of the blood plasma and there is a call upon the tissue fluids to meet the deficit. The ventricular system is very generous in its contributions and pressure in the spinal system falls rapidly. Magnesium sulphate is easy to give and the patients retain it well.

Sodium chlorid on the other hand when given by mouth or vein causes a hypertonic condition of the blood, which draws fluids from the tissues until the entire body is isotonic. Here then after a slight period of reduced pressure there is a secondary salt retention and edema that follows from the excess of the substance in the body. Sodium chlorid, given by mouth, is very irritating and frequently causes nausea and vomiting; even when administered in salol-coated capsules patients complain bitterly.

DISCUSSION

DR. CHARLES H. FRAZIER: The use of magnesium sulphate solution as a substitute for sodium chlorid is, as far as I know, original with Dr. Fay. He has made a very important contribution to the management of intracranial pressure when associated with brain tumors. Not only has magnesium sulphate proved effective when the pressure was due to largely dilated ventricles, but even in the absence of these, and in this particular it may prove of greater value than sodium chlorid. The administration of the latter by mouth has not proved feasible with us, it being most effective when given intravenously. How often one may repeat these injections safely we do not know. Hence to have a substitute in magnesium sulphate, which can be given by mouth or by rectum, and be frequently repeated with perfect propriety, is a matter, I think, of considerable moment.

CASE OF ENDOTHELIOMA OF BRAIN ONE YEAR AFTER OPERATION. DR. WALTER FREEMAN.

This patient, who had previously been in good health complained of inability to use his right hand since 1919, when he noticed twitching of the right side of his face, recurring at intervals of two or three weeks; it was later associated with loss of consciousness. These twitching movements were repeated often, and were accompanied by numbness and tingling in the right hand. Later this hand became clumsy in its movements, with slight weakness; he had to direct it by sight, and was unable to tell the denomination of coins in his pocket. Recently the patient noticed drooping of the right corner of the mouth. In walking he dragged the right leg. There were no involuntary movements of the arm or leg. He had some difficulty in talking, being unable to find the right word. In writing, the characters were formed with great difficulty. Headaches had been paroxysmal, nocturnal and very severe, but were not associated with vomiting. There was no diplopia although the eyesight was becoming poor.

Physical examination revealed drooping of the right side of the mouth with weakness of the right lower facial segment. Power was diminished in the right hand and clumsiness was very marked. The left pupil was larger than the right; both pupils reacted to light and in accommodation, and there was no paralysis of the extra-ocular muscles. The eyegrounds showed choked disk with 3 and 4 diopters of swelling. Astereognosis was present in the right hand although the sensibility (all forms) was retained. The biceps and triceps reflexes were normal on the two sides; the patellar and Achilles reflexes were increased on the right.

Laboratory tests, including roentgen ray and the Wassermann reaction gave no indication of special features and a diagnosis was made of brain tumor of the left side, probably cortical.

Jan. 16, 1922, Dr. Frazier performed an osteoplastic flap exposure over the left rolandic area. On reflecting the calvarium the dura was found extremely tense and very vascular. To relieve intradural tension 15 per cent. salt solution was given intravenously and ventricular puncture was performed. There was immediate relief of tension. The dural flap was reflected and a tumor found growing from the dura and having the reddish granulomatous, vascular appearance of a sarcoma. It did not invade the cerebral substance. It was removed by blunt dissection, hemostasis being secured by silver clips. A section of the dura 6.5 by 8.5 cm. in area was removed with the tumor, and the defect filled with fascia lata graft. Some strips of celloidin were implanted for drainage. Transfusion was performed. The patient was conscious at the end of the operation.

Two days after the operation, the patient began to experience movements of extension of the wrist, about twenty times a minute. These continued for two days and then ceased. There was almost complete loss of power in the right arm, although at the end of five days, some movements were observed when the other arm was exercised. Two weeks after operation there was a fair return of power. The bone flap had ridden up for some unexplained reason and had to be wired down; after this recovery was uneventful.

On discharge, Feb. 11, 1922, it was noted that the patient had no headache, that vision had improved and the swelling of the nerve heads had partially subsided. He had more difficulty in speaking, and greater weakness in the right arm and leg than on admission. At the present time he has regained much of the buoyancy of his walk, his grip is strong, he recognizes objects well, and has no difficulty in talking or writing.

The tumor showed an abundance of cells with many small thin-walled vessels. The cells had large, deeply staining vesicular nuclei and were arranged in whorls. The histologic diagnosis was endothelioma.

GLIOMA OF MEDULLA; REPORT OF CASE WITH EXHIBITION OF SPECIMEN. Dr. Walter Freeman.

The patient, a man aged 41 years, complained of weakness, vomiting and numbness. In November, 1921, he had spells of involuntary movements of the feet. Later he noticed that he fell asleep very readily and was difficult to rouse. His head ached and he felt dizzy. In January, 1922, he began to stagger to the right and seemed to be falling, although he never really fell; yet he could not keep on the sidewalk. In this month he had a severe attack of hiccough that lasted four or five days. Numbness began in his hands and feet on both sides, and he had paresthesias over the back of the head and behind the ears. He had the sensation of "walking on mud." At this time he began to speak thickly and sometimes made mistakes, reversing words or transposing them, although they were all put in and the context would clarify the meaning. He did not omit words or syllables, use the wrong word, skip words, or insert meaningless words in the sentence. For instance, he might say "iron hard" for "hard iron." He was unconscious of these slips at first and blamed his secretary for mistakes she had not committed. He had no aphasia. In reading he would sometimes read parts of paragraphs repeatedly.

In March projectile vomiting began and his eyesight became dim. A curtain seemed to fall before his eyes and things seemed to revolve without disappearing. About March 20, he began to have difficulty in swallowing with regurgitation of liquids through his nose, and saliva collected in his mouth. Shortly before admission, April 14, 1922, he began to bite his tongue. He felt as though he were turning to the right.

Physical examination revealed a well developed adult male of high intelligence. Speech was noticeably thick and he was continuously expectorating saliva. The blood pressure was: systolic, 95; diastolic, 65. There was no choking of the optic nerves; slow nystagmus to the right was present, less to the left. Hearing was normal. The palate appeared to act normally, but the tongue deviated slightly to the right; phonation was irregular. Vomiting and hiccoughing recurred at intervals. The sternomastoids appeared strong but both trapezius muscles seemed weak. There was some weakness of the left extremities with increased reflexes, ankle clonus and a Babinski sign. Sensibility in the limbs, including the sense of position, was normal, but behind the right ear and over the back of the head there was distinct hypesthesia. Spinal fluid was under normal pressure. No spinal subarachnoid block.

Operation was performed by Dr. Frazier, April 21, 1922. On account of the serious condition of the patient, local anesthesia was employed. The usual crossbow incision with suboccipital craniectomy was made. The field was dry, and a very satisfactory exposure was made. It was noted that the right side of the medulla bulged, and this seemed to be due to an intramedullary growth. The operation was concluded with the patient in excellent condition. The systolic blood pressure had risen from 95 to 145 during the course of the operation, and the tongue could now be protruded in the midline.

After the operation, however, the patient was absolutely unable to swallow, had to be fed by stomach tube, and five days later died, apparently from vascular collapse.

The specimen shows an infiltrating growth of the right side of the medulla and upper spinal cord, involving to some extent also the left side. Histologic examination by Dr. Spiller confirmed the diagnosis of glioma.

TWO CASES OF PERIPHERAL NERVE TUMOR. Dr. F. C. Grant.

Case 1.—A man, aged 39, for the past year has noticed a rather rapidly growing lump on the outer side of the right arm just above the elbow. This swelling appeared rather suddenly and he was told that he had a rupture of his muscles. No history of injury or hypodermic injection could be obtained. There was no anesthesia in the forearm or hand, no paralysis and very little weakness in the extension of the wrist and fingers.

A tumor of the musculospiral nerve was diagnosed. At the operation Dr. Ravdin discovered a tumor, 3 by 3 by 8 cm. in size, apparently arising from the sheath of the musculospiral nerve. The brachial radialis muscle was spread out over the tumor. The nerve was dissected free from the tumor without damaging it. The tumor was definitely encapsulated. After removal of the tumor, wrist drop developed with increased weakness of fingers; these disappeared within five weeks after the operation. Dr. Walter H. Freeman of the Philadelphia General Hospital diagnosed the tumor pathologically as a perineural sarcoma.

Case 2.—A woman, aged 46, complained of a lump on the inside of her right arm. Nine years ago she had an injection of typhoid vaccine at this site and for the past three years she has had a small lump in that region. This has gradually increased in size; it is painful to touch and causes pain when her arm is used excessively.

On examination a nodule was found on the inner aspect at about the middle of the right arm. Tingling in the thumb and first finger ensued when it was pressed upon. There was weakness in the same region, but no definite paralysis or anesthesia.

At the operation, an incision was made along the anterior aspect of the arm; the mass was explored and thought to be a neuroma involving, but not severing, the median nerve which passed along the deeper aspect of the growth as a flat band. This was excised with a section of nerve at each end; the severed ends of the nerve were brought together by dissecting down and up, and by flexing the arm at the elbow.

The tumor was circular in shape and about 3 cm. in diameter, well encapsulated and rather firm. It apparently sprang from the nerve sheath and displaced the nerve fibers laterally. The histologic diagnosis was endothelial sarcoma of the median nerve.

A week after operation she presented the typical picture of a median nerve paralysis in the right hand. Complete return of function in the median nerve occurred eight months after operation.

DISCUSSION

Dr. W. W. Keen: There must have been such a wide gap between the two ends of the nerve that I would like to ask how the nerve was anastomosed with such an admirable result in restoration of function.

Dr. Charles H. Frazier: We resort to two methods to compensate for defects, nerve stretching and posture. By continuous stretching over a period of fifteen to twenty minutes we can compensate for 2 or 3 cm. and by flexion of the forearm on the arm, we can compensate for as much more. There are, therefore, really no technical difficulties in overcoming a defect of 4 or 5 cm. Apart from the technical matters, the case interested me as an example of a nerve lesion incidental to the use of hypodermic medication. There have been a number of instances of nerve lesion following introduction of salvarsan. Dr. Dean Lewis of Chicago reported two or three cases not long ago. This feature of the case interests me most, as it is recorded that the woman had received an injection of typhoid vaccine directly over the site of the median nerve; she remembered that shortly afterward she developed weakness in the flexor muscles of the forearm and hand.

VENTRICULOGRAPHY FROM AN EXPERIENCE WITH THIRTY CASES. Dr. F. C. Grant.

This will be published in full in a later issue of the Archives.

Book Reviews

NERVOUS ILLS, THEIR CAUSE AND CURE. By Boris Sidis, M.A., Ph.D., M.D. Cloth. Price $3 Net. Pp. 379. Boston: Richard G. Badger, 1922.

This book has not a few merits, not the least of which is its criticism of Freud and the Freudians. The author says that psychanalysis, with which term Freud and his adherents have baptised their sexual theories and metaphysical wish-speculations, is savage and barbaric. Dr. Sidis' own thesis is much simpler. For him the impulse of self-preservation is at the basis of all animal life. He well says (p. 19) that from the simplest lump of protoplasm, constituting a microbe, to the highest form of life, such as man, one meets with the same primitive life tendency—the impulse of self-preservation. Throughout all animal creation one important purpose runs, and that is the preservation of life. This impulse has two aspects, a positive and negative. In the positive form the impulse is to keep the individual alive; in the negative, to preserve the individual from injury and death. This negative impulse expresses itself in the form of *fear*. It is the morbid activity of this instinct of fear that lies at the root of all the nervous ills. This, in brief, is the thesis that is expounded by Dr. Sidis.

In some, if not all, of this we are at one with Dr. Sidis. The emphasis put on sex by Freud and his imitators is mischievous and misleading. There are other instincts than the instinct of sex. The Great War clearly proved (what, indeed, needed no proof for any observing man) that the instinct of self-preservation, with its attending emotions of fear, cowardice, self-respect and self-reproach, is far more potent than the instinct of sex to cause the gravest psychoneuroses. But since the war made this truth so manifest it would seem that the time had come for these writers to keep their minds of sexual subjects, for a while at least. Dr. Sidis' book will help them to do this, and we believe that its influence in this respect will be altogether for good.

Dr. Sidis holds that fear is not a matter of belief. It is one of the most fundamental of animal instincts, having its roots deep down in the organism. Throughout his book he traces the action for good and evil of this fear instinct, and he does it, in the main, in an interesting and illuminating way. It is this that gives his book a truly philosophic tone.

The inferences which he draws from this idea in the domain of mental pathology are always engaging and often convincing. For Dr. Sidis this instinct of fear—this disturbance or perversion of the instinct of self-preservation—is the root of all evil. Whether the reader always agrees with him or not, he will find much that is novel and suggestive in the author's treatment of this subject. For our part we agree with him very often, and do not hesitate to recommend his book to neurologists.

We wish we could say that the book had no faults, but in this respect it is a very human document. Although he disclaims being a psychanalyst, Dr. Sidis has some of the faults of that cult. The chief of these is his use sometimes of a very obscure and cumbersome phraseology. He evidently belongs to those who think they can venture at will into the dark realms of the subconscious. This does something to spoil his writing for us. When we met with the sen-

tence, "abnormal suggestibility is a disaggregation of consciousness," we were tempted to throw down the book in despair; and when a few pages later we read something about "reintegration in consciousness," we were not much encouraged to continue. Such words have no meaning for us, and we wish that the author had seen fit to clothe his ideas—which indeed are very plain and simple—in a plain and simple style.

But Dr. Sidis is not always obscure. He describes, with a truly dramatic touch, the supreme selfishness of psychopaths. The paranoidal impulse in them is expressive of the disturbed instinct of self-preservation and fear. He thus denies an "inferiority complex," and says that the patient's real mental state is fear that his sense of superiority will be humbled. But is not this paranoid mood a sort of "defense reaction," as expressed in the lingo of the present day?

Much importance is attached to what the author calls the "hypnoidal" state, which is apparently the stage 'twixt sleep and wake, and is the same that some older writers have called the "predormition." At least, so it appears to us, although Dr. Sidis may not acknowledge the identity, for he claims the merit of having originally described and utilized this state. It is not a state of true hypnosis, although one apparently in which suggestion is easily used.

We do not quite agree with Dr. Sidis in his rather caustic criticism of the doctrines of heredity, but we think he is probably right in his poor opinion of eugenics. It is indeed refreshing to have some one speak up plainly and tell us what he thinks about the craze for legalized eugenics, which is only another name for universal maternalism.

We think that Dr. Sidis' book is too long. It contains too many tedious case reports, and is full of repetitions. It could easily have been compressed into one half the space, and much improved by the process. In saying this we are speaking for a neurologic world which is harassed by a multiplicity of writings. But it is a book worth reading.

THE KINGDOM OF EVILS; PSYCHIATRIC SOCIAL WORK PRESENTED IN ONE HUNDRED CASE HISTORIES TOGETHER WITH A CLASSIFICATION OF SOCIAL DIVISIONS OF EVIL. E. E. SOUTHARD, M.D., and MARY C. JARRETT, with an Introduction by Richard C. Cabot, M.D.; a Note on Legal Entanglement as a Division of Evil, by Roscoe Pound; and an Appendix on Legislation in Relation to Mental Disease, by Frankwood E. Williams, M.D. Cloth. Price, $5.50. Pp. 708. New York: The Macmillan Company, 1922.

This book with its long and characteristic title was not quite completed at the time of Dr. Southard's death. It is evident that the affection of his friends gathers round his memory.

Book I gives full case records in an attempt to describe the public, social, and individual spheres of social work. Book II has as a special feature a division of "The Kingdom of Evil" into five states, Disease, Ignorance, Vice, Legal Entanglement, Poverty. The last five of thirty-eight illustrative records are examples of so-called pure types of each kind of evil, though the comment shows that the authors recognize that types are never entirely pure. The example of a problem in "Ignorance" follows: John Henry, aged 15, was rescued from a dark cellar where his mother had kept him for five months. His mother previously had kept him back at school and persuaded the teachers that he was feebleminded. The poverty-stricken family had moved eleven times in five years, and he had been kept from contact with other children. All this did not prevent him from receiving a mental rating of 16 years on the Yerkes-

Bridges point scale and of 15 years, 1 month on the Stanford-Binet scale. The records given in Book III illustrate eleven major forms of mental disease. Before leaving the subject of this "quarry" of case record material, attention should be called to three unrevised records of the Psychopathic Hospital social service in the appendix; the first is eleven pages long, the second forty-nine pages, and the third thirty-eight pages.

In Book IV there is a change from detailed description to the laying down of principles, and to comment on social work in general. Dr. Southard regards the chronic insane as "a comparatively small group of unfortunates," though they are the main interest of state hospitals and state laws. His interest spreads to the psychopaths, the eccentrics, those very slightly subnormal, and to the supernormal. "One out of every two cases of social trouble is a psychiatric case." And so "psychiatric social work can establish and is now establishing new principles for social work in general."

In the discussion of the problem of Evil, Dr. Southard's interest in and dependence upon Professor Royce is in evidence, and gives the clue to the choosing of the quotations from Job with which the book is sprinkled. His passion for playing with definitions brings a many faceted dealing with the Grail hunters and the dragon killers, the rebuilders and the destroyers in our public life, the alienist as distinguished from the psychiatrist, the sociologist from the physician, and the contrasting aims of nurse, social worker, and psychiatric social worker. The reader is told particularly how the technic of psychiatric case work could be applied to war, bolshevism, and industry. There is both interest and incompleteness in this book. It shows psychiatry in its present state of transition.